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The Journal of Pediatrics

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Original Communications

VITAMIN A DEFICIENCY IN INFANTS

A CLINICAL AND PATHOLOGICAL STUDY

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INTRODUCTION

INTRIGUED by the number of undernourished infants in whom histopathologic lesions characteristic of a lack of vitamin A have been found at necropsy when the disease had escaped detection during life, a review of the case records of 13 patients observed in this clinic during the past ten years, has been made with the purpose of: (1) directing attention to the relative frequency with which specific lesions are found in the epithelial lined tissues of the body before recognizable external evidences become apparent and (2) pointing out certain criteria whereby the diagnosis of this clincal entity may be facilitated.

Before turning to the results of this analysis, a brief summary is presented dealing with knowledge referable to vitamin A deficiency, which has accumulated from the extensive investigations conducted during the past few years, in both man and animals.

Hopkins[1] was the first to recognize that animals could not live on a diet of pure protein, fat, carbohydrate, and water, even when the necessary inorganic materials were provided. When a small amount of milk was added, however, normal growth was restored. He proved that this property of milk was dependent on an alcohol-soluble substance and was not due to the other essential elements. A few years later, Osborne and Mendel[2] and almost simultaneously McCollum and Davis,[3, 4] likewise found that cow's milk possessed a disease protecting

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substance which was fat soluble.* Osborne and Mendel[5] made the further, and more far-reaching, observation that the white rat, when kept on a diet lacking in fat-soluble A, became emaciated and developed a characteristic *ophthalmia* which was cured promptly by the addition of either butter fat or cod liver oil. As the result of these experimental studies, it was established that in order to maintain normal nutrition there are required other substances than protein, fat, carbohydrate, water, and salts, and that a deficiency of these accessory food substances or vitamins results in "nutritive failure and disease."

Stimulated by the discoveries of physiologists and chemists, and as a consequence of the readiness with which vitamin A deficiency could be produced in small laboratory animals, it was not long before the underlying histologic changes became clarified by pathologists. Wolbach and Howe[6] were among the first investigators to throw light on this phase of the subject. They demonstrated in the albino rat and in the guinea pig that the specific effect of a deficiency of vitamin A involved the epithelial-lined structures of the body with the substitution of stratified keratinizing epithelium for normal epithelium. Furthermore, Wolbach and Howe showed that the so-called "abscesses" which had been noted by practically all experimental workers and generally taken as evidence of infection, consisted of collections of keratinizing epithelium "in the alimentary and respiratory tracts, in the submaxillary glands, the parotid glands, and the accessory salivary glands of the tongue and pharynx; in the genitourinary tract and in the reproductive system. Of the ductless glands, the thymus alone shows specific changes." In man, while the histologic processes involving the eye have been described in detail, little attention in the majority of the cases reported in the literature has been paid to the epithelial reaction elsewhere in the body. Usually the clinical and anatomic diagnosis given has been "malnutrition, keratomalacia, and bronchopneumonia."[7] That the histologic changes in infants are comparable to those found in animals when the disease is produced experimentally has been shown by Wilson and Dubois[8] and has been confirmed by Thatcher and Sure[9] and others.

As a result of the high incidence of infections which occur in vitamin A deficiency disease in both man and animals and with the impression gained in the treatment of disease with vitamin A or its concentrates, the suggestion has been made that this substance acts as an anti-infective agent. With regard to this highly controversial question, until more exact experimental and clinical proof is available, it would seem advisable to accept the opinion advanced by Eusterman and Wilbur[10] that "vitamin A is a physiologic prophylactic against infection, by virtue of the fact that it maintains the integrity of the

*Later, as is well known, McCollum and his coworkers established the fact that there was another specific element associated with the fat-soluble substance which had the property of enhancing the deposit of calcium, vitamin D.

epithelial linings of the mucous tracts and the skin, but its 'anti-infective' function, that is, its ability to cure infections when the barrier of mucous membranes has been passed, or to prevent or cure infections of the blood stream is not yet established."

Prior to the epoch-making discovery by Hopkins in England and by McCollum and Davis, and Osborne and Mendel, in this country, clinicians had recognized the association of noninflammatory lesions of the eye with severe malnutrition. As early as 1857, Mackensie[11] wrote, "In particularly emaciated infants I have seen . . . the cornea of one or both eyes . . . perforate with almost no evidence of inflammation." In 1892, Spicer[12] reported that the eye disease was dependent probably upon the lack of nitrogenous elements in the diet. Nearly twelve

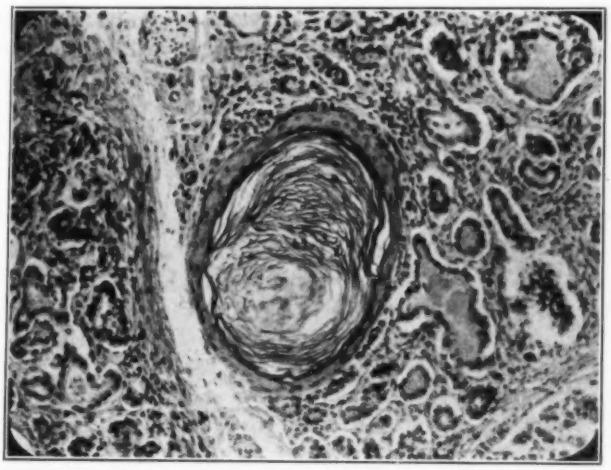

Fig. 1.—Photomicrograph of section of pancreas (Case I). Note metaplasia of lining epithelium and desquamated keratinized cells occluding one of pancreatic ducts. Hematoxylin and eosin. High power.

years later (1904), Mori[13] described a like condition in 116 children from two to five years of age. These children were breast fed during the first year, after which time their diet consisted mainly of cereal and vegetables. Mori thought the eye condition resulted from a lack of fat in the diet and that the specific curative action of cod liver oil was due to its bile constituents. In 1906, Czerny and Keller[14] also referred to corneal ulceration as a complication of "Mehlnährschaden."

The investigations of Professor Bloch,[15] considered in the light of the newer knowledge of vitamin A, are of special importance. In 1917, he attributed xerophthalmia, or keratomalacia in infants with general malnutrition, to the lack of special substances which were contained in certain fats. Likewise, he showed that curative effects were brought about by the replacement in the diet of substances contained in milk

and especially in cod liver oil. Bloch called attention also to the close parallelism existing between the clinical manifestations in children, especially during the early years of life, and the findings in experimental animals (albino rats). The expected sequence of events is a decline in weight and inactivity with the physical evidences of atrophy of the tissues; an increased susceptibility to infection of the regional systems of the body (the alimentary, gastrointestinal, and genitourinary systems), and finally the appearance of dryness of the conjunctivae (xerosis) and necrosis of the corneae (keratomalacia or xerophthalmia).

However, exceptions to the above sequence of events occur. The extreme variability of the clinical and pathologic manifestations in man and in the same and different species of animals, constitutes one of the perplexing peculiarities of this disease, and is a matter which has an important bearing on that phase of the subject under discussion. For instance, on a diet inadequate in vitamin A, an animal may not cease to grow within the expected time, or children whose nutrition is otherwise normal may present "night-blindness with no other symptoms of the disease except lassitude." Even histologic evidences instead of involving the epithelial structures in an orderly manner, may be revealed in only one or perhaps a few sites. Conversely, on a diet supposedly adequate in vitamin A, symptoms of avitaminosis may be present, as has been observed clinically and by detailed microscopic examination of the tissues.

How may these variabilities be accounted for? In the first place, vitamin A is not synthetized in the animal organism so the amount available for immediate use and for storage in the liver and other tissues, to meet the minimum needs of the body, depends on the amount as such or its precursor carotin, contained in the food consumed. Therefore, the amount stored may vary from time to time, in man and in different animal species. Second, the exact chemical nature is not known, but usually vitamin A is associated intimately with fats, and its release is dependent on their solubility. Therefore, those mechanisms interfering with the solubility, together with incomplete absorption and assimilation of fat, curtail materially the amounts of vitamin A available for storage and utilization. Undoubtedly as further information is secured regarding the relationship between vitamin A and carotin, the precursor of vitamin A (and their chemical nature), clarification of the pathogenesis of this disease may be expected.

Passing now to a consideration of the cases herein reported, the patients were full-term infants, with the exception of one, who was born prematurely. Eight were males and 5 were females. They varied in age from one to eighteen months; 11 patients ranged from three to nine months and the remaining patients were eighteen months and one month old, respectively. It will be in place to mention here the essen-

tial features in the case of the one-month-old infant (Case 2) because of the rarity of this disease at so early an age. He had been breast fed exclusively. "Snuffles off and on" had persisted since birth, and he had not gained as regularly as the other children. He was taken ill three days before admission and died twelve days later of "diffuse bronchopneumonia" with multiple abscesses in the lungs. Except for a moderate degree of undernutrition, examination revealed no clinical sign suggestive of vitamin A deficiency, but at necropsy, in addition to the extensive process in the lungs, keratinization of the epithelial cells was found in the trachea and tracheal glands and pancreatic ducts on microscopic examination.

It is of particular interest to note that in this series of cases the clinical diagnosis was established correctly in 6 patients by the presenting eye sign, keratomalacia. In 7 of the 13 patients the diagnosis was established *histologically* at necropsy; clinical manifestations of vitamin A deficiency disease were not present during life. The clinical diagnosis in 5 of these 7 patients was diffuse lobular pneumonia as a coexisting manifestation of a chronic disorder of nutrition. Of the other 2 cases one patient was suffering from congenital obliteration of the bile ducts, and one patient with eczema and pansinusitis.

Twelve patients died; one patient recovered with a permanent visual disorder. Necropsy was performed on 11 patients* and the histologic diagnosis of vitamin A deficiency disease was based on the finding of keratinized epithelial cells in one or more epithelial-lined structures in the body.

PATHOLOGY

Inasmuch as the postmortem recognition of the consequences of vitamin A deficiency is not always easy, an outline of the pathology is indicated before we discuss the individual cases of this report.

The initial effect of vitamin A deficiency in rats and guinea pigs is upon epithelial structures and is, therefore, to be regarded as the specific effect. This primary consequence may be regarded as a specific starvation of epithelium resulting in atrophy and finally by replacement with stratified keratinizing epithelium, identical in all locations and arising from focal proliferations of basal cells. This metaplasia has also been found in infants, the monkey and mouse; and gross changes described in various publications indicate that it also occurs in swine, dogs, rabbits, calves, and the domestic fowl. As has been pointed out by one of us, it seems evident that vitamin A is essential in most vertebrate species and that its withdrawal is followed by a common effect upon epithelial structures, regardless of species.

The experimental work of Wolbach and Howe[16] shows that the keratinizing metaplasia is a repair phenomenon stimulated by *atrophy* of

*The clinical diagnosis in the other two patients was based on the pathognomonic sign, keratomalacia.

the original epithelium. This reparative response takes place in the basal cells which are the only cells capable of proliferation in epitheliums with secretory functions.

While the keratinizing metaplasia produces impressive gross lesions in infants and in experimental animals due to the occlusion of ducts by desquamated keratinized cells and consequent cyst formation, it must be remembered that this is a late effect; in fact, the consequence of attempted repair following atrophy of essential epitheliums. Therefore, we should consider effects upon the organism as a whole which must follow reduced activities of many epitheliums preceding the stage of complete atrophy and metaplastic replacement.

These general or secondary effects of vitamin A deficiency are of course those observable in infants during life, long before the only external specific effect becomes apparent; that is, the hyperkeratinization of the corneal epithelium and the consequent ophthalmia—always a late consequence even in animals and rarely producible in the otherwise very susceptible guinea pig.

We may list the secondary effects of vitamin A deficiency common to both infants and laboratory animals as follows: (1) loss of weight due largely to loss of fat in all storage depots, but also to atrophy of musculature and many organs; (2) anemia; (3) cessation of growth of bones; (4) degenerative changes in skeletal muscles; and (5) lymphoid hypoplasia.

The loss of fat in experimental animals in the absence of vitamin A takes place in spite of a liberal amount of fat in the diet, and as it is well established that normally there is a store of vitamin A in fat tissue, *rarely is an abundance of stored fat compatible with the diagnosis of this deficiency.*

The anemia in infants, rats, and guinea pigs is accompanied by hemosiderosis of the spleen and liver and in prolonged deficiencies by an atrophy of the spleen and bone marrow. The hemosiderin is found in the spleen, phagocytes, the reticular cords, and in the sinuses. It is found in the liver in cells lining the sinusoids and in the liver cells. In animals, restoration of the diet is followed by regeneration of the bone marrow, disappearance of the hemosiderin from spleen and liver, and in the rat also in the spleen by an active hyperplasia of lymphoid structures and an outburst of erythroblastic activity.

The cessation of growth of bones is accomplished by cessation of proliferative activities on the part of the epiphyseal cartilage. This results in a narrow band of atrophic cartilage which on the diaphyseal side becomes bounded by a thin plate of bone. In recovery the cartilage regenerates, and blood vessels from the diaphyseal side penetrate the limiting bony plate and enter the cartilage cells to form the normal trabeculations of growing bone.

Other changes, such as degenerations of the skeletal muscles and lymphoid hypoplasia have been poorly studied. We have noted degeneration of voluntary muscle fibers in the infants of this series, incidentally, in the course of the histological studies, and hence in the muscle accompanying the sections of the neck organs, ribs, and diaphragm. In laboratory animals the lesions of skeletal muscles may be extensive and striking, and terminate in calcification. However, in both infants and animals there is nothing distinctive about the muscle changes. They are in sequence, loss of striations and swelling of muscle fibers, resulting in hyalin masses which subsequently autolyze or become calcified.

The lymphoid hypoplasia is most evident in the spleen. In lymph nodes draining infected keratinized cysts, enlargement may be found

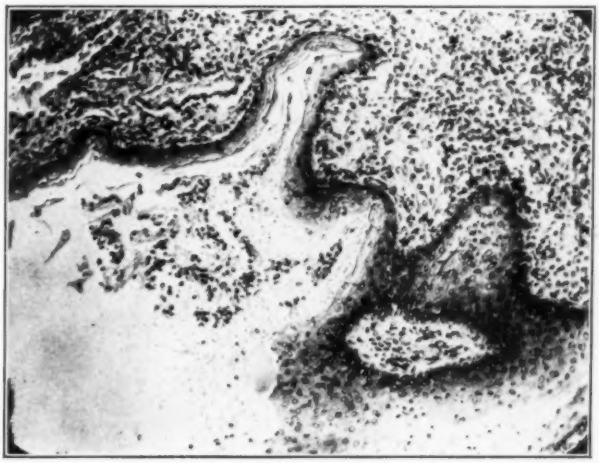

Fig. 2.—Photomicrograph of section of lung (Case I) showing stratified squamous epithelium in small bronchus. Hematoxylin and eosin. High power.

but, in general, the lymph nodes are inactive. Although epithelial metaplasia is a late consequence of vitamin A deficiency, its demonstration is essential for the postmortem diagnosis of the condition. Whether there are other causes of keratinizing metaplasia in infants remains to be determined, long-continued inflammations for example.

In all instances in which we have made the postmortem diagnosis of vitamin A deficiency, we have found in addition to keratinizing metaplasia in one or more epitheliums, gross and microscopic evidences of fat resorption and hemosiderosis of the spleen.

In evaluating the importance of epithelial metaplasia we must keep in mind that its presence in any one location is probably indicative of profound physiologic disturbances in many locations, often indicated

by microscopically demonstrable diminution in size of cells. *The keratinizing metaplasia follows a nonviable degree of epithelial atrophy.* Undoubtedly responsible for the profound growth and nutritional consequences are degrees of atrophy and consequent physiologic inefficiency which precede the keratinizing metaplasia.

In infants the commonest and earliest appearance of the keratinizing metaplasia is in the trachea and bronchi. Next in frequency and sequence is the pelvis of the kidney. The respiratory mucosa of the nares and accessory sinuses in the one instance examined showed the characteristic metaplasia, and as these regions are constantly and early affected in rats and guinea pigs, we may assume that in human beings,

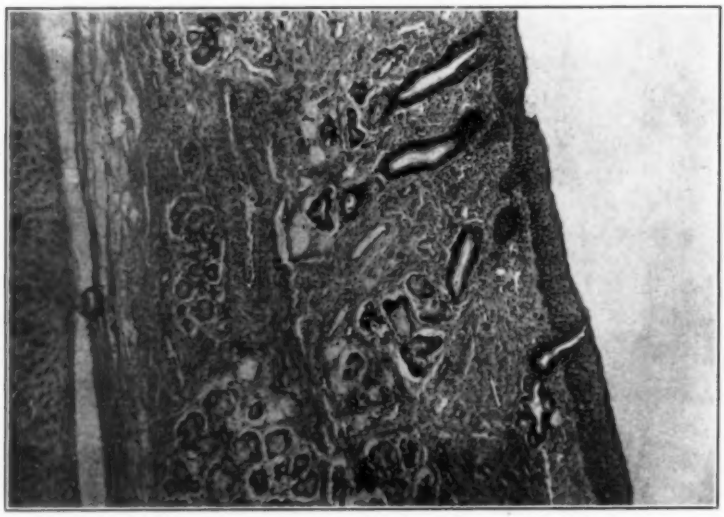

Fig. 3.—Photomicrograph of section of nasal mucosa (Case 10) showing metaplasia of epithelium. Hematoxylin and eosin; ×115.

epithelial atrophy and metaplasia are important features in the production of disease of these by-ways of the respiratory tract.

The early effect of the deficiency upon the respiratory mucosa is, in our minds, a satisfactory explanation of the frequency, severity, and persistence of the pneumonias that have been in most instances responsible for death.

The type of pneumonia is one apparently beginning with bronchitis, followed by interstitial invasion of the lung by the pathogenic microorganisms. While in rats and guinea pigs which had been shielded from sources of infection we often found complete keratinizing metaplasia of trachea and many bronchi before infectious processes became apparent, in infants infection and invasion have been present in sev-

eral instances with only the minimum amount of metaplasia. As in rats and guinea pigs, bronchiectatic cavities were constant, and we regard the atrophy first, and finally the metaplasia as important features in the production of bronchiectasis. We have in rats and guinea pigs, subsequent to the loss of the ciliated epithelium, demonstrated the inhalation of starch granules into the pulmonary alveoli. Presumably the same factor is of importance in human beings, in permitting particles to reach the alveoli of the lungs. In rats and guinea pigs, we believe that the initial infection of the lungs often takes place in regions in which the bronchioles have been obstructed by the accumulation of desquamated keratinized cells. Bronchiectatic cavities filled with these cells have been found in rats and guinea pigs without microscopic evidences of the presence of infection. In our cases actual blockage of bronchioles by desquamated keratinized cells probably occurred in Cases 1 and 10, but the important predisposing factors to infection are, in our opinion, *loss of protective powers of the epithelium due to diminished or absent mucous secretion and loss of ciliary motion.* Other consequences of the atrophy not demonstrable may be concerned.

Six of the 11 cases studied at postmortem showed extensive pancreatic lesions, all identical and presumably representing a disease entity. At first we regarded the pancreatic changes as the result of vitamin A deficiency. As the same condition has been found scores of times without other evidences of vitamin A deficiency and since it is not constant even in severe vitamin A deficiency, we must consider the two as not necessarily connected.

The pancreatic lesion referred to is characterized by dilatation of acini and ducts, by inspissated secretion, atrophy of the acini, lymphoid and leucocytic infiltration to some degree, and fibrosis. Our preliminary studies indicate that the pathogenesis of this striking pancreatic affection resides in the production of an abnormal secretion which inspissates and leads to distention and atrophy of ducts and acini. It is reasonable to assume that this pancreatic lesion, if extensive, may be responsible for the failure to utilize fats and hence vitamin A in the presence of an adequate intake.

The demonstration of irrefutable evidences of vitamin A deficiency in Case 11, in view of its feeding history may well be regarded as due to failure of assimilation rather than of intake of vitamin A in consequence of the congenital atresia of the common duct.

Case 9 is another example of probable failure of the patient to utilize an adequate amount of vitamin A in the diet, inasmuch as the histologic findings were those corresponding to the early recognizable stages of the deficiency. The long history of eczema and the relatively long period of adequate diet while in the hospital warrant the conclu-

sion that failure of assimilation was responsible for the recently acquired evidences of vitamin A deficiency.

CLINICAL AND PATHOLOGIC REPORTS OF CASES

CASE 1.—Infant No. 10,465; Necropsy No. 1009. The patient, a female infant of five months, was admitted to the hospital on account of recurring respiratory infections, and failure to gain in weight of three months' duration. Vomiting and diarrhea were not conspicuous symptoms. Weight at birth: 6½ pounds. Weight on admission: 6½ pounds. The weight-height ratio was 0.32 as compared with 0.60 for the normal for this age. Temperature: 102.4° F.

Diet: The infant had received breast milk and cow's milk for one month and a diet of evaporated milk and water exclusively for four months. Cod liver oil and orange juice had not been given.

Examination revealed an extremely underdeveloped and undernourished infant; signs of diffuse infiltration throughout both lungs, and consolidation of the upper lobe of the right lung; dryness of the sclera, ulceration of the cornea and after five days, perforation of the cornea with the development of a bilateral hypopyon.

Roentgenogram: Consolidation in upper lobe of the right lung. *Blood:* Hemoglobin 90 per cent; R.B.C. 4,290,000; W.B.C. 29,000. *Urine:* Negative.

Comment.—This patient who had received a diet inadequate in vitamin A, failed to grow, suffered from repeated respiratory infections which were followed after four months by the typical picture of xerosis of the conjunctivae and keratomalacia.

Necropsy.—This case with the postmortem examination was reported by Wilson and Dubois in 1923.[8] The immediate cause of death was bronchopneumonia of the type beginning with bronchitis and peribronchitis (interstitial pneumonia), and accompanied by extensive bronchiectasis formation. Keratinizing metaplasia of epithelium was found in the trachea, bronchi, salivary glands, pancreas, pelvis of kidney, and uterus. Bronchiectatic cavities were also lined with keratinizing stratified epithelium. Other findings such as are constantly present in experimental animals in vitamin A deficiency were microscopic evidences of fat resorption and hemosiderin deposits in phagocytic cells in the spleen and in hepatic and sinusoidal cells in the liver.

CASE 2.—Infant No. 10,977; Necropsy No. A-24-18. The patient, one month old, was admitted to the hospital on account of a respiratory infection of three days' duration. Birth weight: 7 pounds. Weight on admission: 6 pounds 12 ounces. The temperature: 99.8° F.

Diet: Breast feedings since birth. Cod liver oil and orange juice had not been given.

Examination revealed a well-developed and fairly well-nourished male infant with respiratory embarrassment, cyanosis, and cough of a metallic quality. Resonance was impaired over the entire chest, and the breath sounds were increased in intensity. Râles were not present. The eyes were normal. During the following few days the patient became progressively worse and died on the tenth day.

Rontgenograms showed clouding of the upper lobe of the right lung. *Blood:* Hemoglobin 85 per cent; R.B.C. 4,200,000; W.B.C. 21,000; Polymorphonuclears 75 per cent. *Urine:* Negative.

Comment: The infant, although being fed at the breast, had gained slowly, and in the history it is stated that he had had "snuffles" and a slight cough since birth. The diet was regarded as affording an adequate supply of vitamin A, although, inasmuch as he had not gained, it is possible that the mother's milk was inadequate in quality and quantity. No external evidences of vitamin A deficiency were detected.

Necropsy.—The immediate cause of death was extensive bronchopneumonia of the type beginning with bronchitis and peribronchitis. There were numerous bronchiectatic cavities, some of them with the epithelium partially destroyed. Keratinizing metaplasia was found in the trachea and tracheal glands and to a very slight degree in a pancreatic duct. Other findings constant in vitamin A deficiency were hemosiderin deposits in phagocytic cells in the spleen and in hepatic and sinusoidal cells in the liver, and microscopic evidences of fat resorption. The pancreas showed marked atrophy of the acinic cells with a diffuse increase of connective tissue cells. Most of the ducts were dilated and filled with concentrically laminated material; the epithelium appeared atrophic and flattened. This laminated material in the ducts stained deeply with eosin. Many gland acini also contained a similar laminated though faintly stained material. The appearances suggest that this material was produced in the gland acini and represents an inspissated secretion. This pancreatic lesion is not peculiar to vitamin A deficiency and has not been seen in laboratory animals with experimental deficiency.

CASE 3.—Infant No. 11,065; Necropsy No. A-24-28. The infant, a male aged four and a half months, was admitted to the hospital because of a cough of three and a half months' duration and failure to gain in weight. There was a history of frequent vomiting and diarrhea following the onset of infection at one month of age. Weight: 5 pounds. Weight-height ratio 0.22 as compared with 0.62, the normal for the age.

Diet: He was breast fed for one month and then given a formula containing from 10 to 12 ounces of milk a day. Cod liver oil and orange juice had been given.

Examination: He was an extremely emaciated baby, breathing rapidly and with difficulty, with râles distributed throughout both lungs. Eyes were normal. The baby died within five hours after admission.

Comment.—The infection of the respiratory tract with failure to gain, especially with vomiting and diarrhea, might, in the light of the present knowledge regarding vitamin A deficiency, have suggested vitamin A deficiency, but neither xerosis of the conjunctivae nor keratomalacia were noted. The amount of whole milk, with orange juice and cod liver oil daily, was believed to be sufficient for protection against vitamin A deficiency disease.

Necropsy.—The immediate cause of death was bronchopneumonia of the type beginning with bronchitis and peribronchitis. There were many bronchiectases and a few bronchiectatic abscesses.

The trachea showed only keratinizing metaplasia and here the process was early. The spleen contained deposits of hemosiderin in phagocytic cells. The pancreas showed atrophy and fibrosis with laminated inspissated secretions in acini and in dilated ducts lined with atrophic flattened epithelial cells.

Fat cells in various locations were largely devoid of fat and had reverted to the embryonic type.

CASE 4.—Infant No. 14,541; Necropsy No. A-28-139. The patient, a white, male infant, three and a half months old, was admitted because of loss of weight of one month's duration. He was one of twins,* born one month prematurely, and weighed 4 pounds at birth. One month prior to admission he developed a rather severe "respiratory infection" and began to refuse his formula and vomit whenever it was forced. Two weeks before admission, "white opacities" appeared in each eye. The weight on admission was 5 pounds 6 ounces. The weight-height ratio was 0.27 as against 0.47, the normal for this age. The temperature was 98.6° F.

*The twin brother died two weeks before the admission of this baby with a similar condition. This case is not included in the series.

Diet: He had never been breast fed, the diet consisting of boiled condensed milk and water. Neither cod liver oil nor orange juice had been administered.

Examination revealed an emaciated male infant with labored breathing and dusky color. Both eyes showed keratomalacia, and there were signs of a diffuse infiltration in both lungs. Following treatment, the patient improved steadily until during the fifth week after admission when there was a recurrence of the signs of pulmonary infection which resulted in death.

Roentgenograms: Lungs showed diffuse, quite dense infiltration, generalized but marked in midportions and in the upper right lobe. After treatment of ten days: Considerable amounts of very dense infiltration, but definite clearing. *Bones:* Increase in density of metaphyseal margin of long bones. *Blood:* Hemoglobin 70 per cent; R.B.C. 4,520,000; W.B.C. 39,300; Polymorphonuclears 58 per cent. *Urine:* Negative.

Comment.—An infant three and one-half months old, who had never received breast milk, fresh cow's milk, or vitamin A substances developed the typical picture of keratomalacia, after being fed condensed milk about three and one-half months. He showed signs of respiratory infection prior to the development of the typical eye signs.

Necropsy.—The immediate cause of death was extensive bronchopneumonia, active in some portions of the lungs, organizing in others. The type was that secondary to bronchitis and peribronchitis of a progressive character. Acute alveolar emphysema and interstitial emphysema were present in portions of both lungs.

Owing to the fact that this infant was treated during its five weeks' residence in the hospital for vitamin A deficiency, little evidence remained of the metaplasia of epithelium which characterizes this condition.

Familiarity with the details of epithelial repair in recovery (Wolbach and Howe[16]) enables us to state that there had been keratinizing metaplasia in bronchi and renal pelvis. Persistent metaplasia was found in glands and their ducts in the larynx.

Microscopic evidences of fat resorption were present in many locations. There was slight hemosiderin pigment deposit in the spleen, none in the liver.

CASE 5.—Infant No. 316,268; Necropsy not obtained. The patient, a male infant of five and a half months, was admitted with a history of failure to gain since birth. As a consequence of a multiplicity of congenital malformations (brain, heart, meningocele) feeding had been difficult.

Diet: He had never been breast fed on account of cyanotic attacks when attempting to nurse. He was offered whole milk daily in adequate amounts, but (because of difficulty in feeding) all or a part of each feeding was refused. Cod liver oil had not been given regularly.

Examination: Whereas the baby weighed 7 pounds 12 ounces at birth, when first observed in this clinic, he weighed 6 pounds 4 ounces. He was an extremely emaciated baby with moderate respiratory distress, showing the classical signs of keratomalacia. There were multiple congenital anomalies of the central nervous system and cardiovascular system.

Roentgenogram: Slight infiltration of both lungs. *Blood:* Hemoglobin 55 per cent; R.B.C. 3,850,000; W.B.C. 7,200; Polymorphonuclears 50 per cent. *Urine:* Negative.

Comment.—During his stay in the hospital, he gained only 1 pound 2 ounces in four months, despite efforts directed toward supplementing his diet with maximum amounts of cod liver oil by mouth and food rich in vitamin A by gavage. The development of keratomalacia in this patient presumably was the result of subminimum quantities of vitamin A occasioned by refusal to eat, and vomiting. The patient died subsequently of bronchopneumonia. Necropsy was not obtained.

CASE 6.—Infant No. 16,626; Necropsy No. A-30-241. The patient, a male infant of eighteen months, was admitted to the hospital because of cough and discharge from the ears of three weeks' duration. Neither vomiting nor diarrhea had been present before the acute infection presented. Weight: 16 pounds. Weight-height ratio was 0.54 as contrasted with 0.77, the normal for the age. Temperature: 103° F.

Diet: The history records that he was breast fed for four months and was then given a cow's milk formula to which was added subsequently other articles of food. It is stated that he received cod liver oil and orange juice irregularly.

Examination revealed undernutrition and signs of diffuse bronchitis and otitis media. The eyes were normal.

Roentgenogram: Moderate amount of diffuse congestion, particularly in the right lung, with a small amount of fluid. *Blood:* Hemoglobin 50 per cent; R.B.C. 4,140,000; W.B.C. 15,250; Polymorphonuclears 70 per cent. *Urine:* Albumin +, no formed elements.

Comment.—Death occurred after an illness of about three weeks' duration from an acute generalized infection, involving the respiratory and gastrointestinal tracts and with thrombosis of the cerebral sinuses. An atypical paratyphoid bacillus was recovered from the blood. The diet would appear to have supplied him with an adequate amount of vitamin A. There were no external evidences to suggest vitamin A deficiency disease.

Necropsy.—The immediate cause of death was bronchopneumonia with bronchiectatic abscesses and empyema. The pneumonia was accompanied and presumably preceded by a severe bronchitis and peribronchitis. There was also a terminal ulcerative colitis and blood stream invasion by paratyphoid bacillus.

Keratinizing metaplasia was found in the trachea, bronchi, and in the ducts of the esophageal glands. Reparative processes were apparent in the trachea, presumably induced by approximately three weeks of hospital diet.

The spleen and liver were free from hemosiderin deposits.

Fat from several locations showed microscopic evidences of resorption.

CASE 7.—Infant No. 17,305; Necropsy No. A-31-143. An infant, nine months of age, was admitted to the hospital because of refusal of food and cough of four weeks' duration. Birth weight: 6 pounds 11 ounces. Weight on admission: 11 pounds 13 ounces. Weight-height ratio 0.47 as compared with 0.69, the normal for this age.

Diet: During the first six months of life, the infant vomited projectilely from one to four times a day, and great difficulty was encountered in feeding him. He was never breast fed but received various dilutions of cow's milk with added carbohydrate. From six to nine months of age he received one quart of "Vitamin milk" from which a small amount of cream was removed, daily. Small amounts of cod liver oil and orange juice had been given daily since the baby was two weeks old. An unstated amount of viosterol had been given each day during the last three months. Fresh vegetables, soups, and broths had been refused.

Examination revealed a poorly nourished, white, male infant, with rapid respiration, profuse nasal discharge, and signs of a diffuse pulmonary infection. The conjunctivae and corneae were normal. The pulmonary infection became progressively worse and nine days after admission the patient died.

Roentgenogram: Infiltration of both lungs without evidence of consolidation. *Bones:* Increased density of metaphyseal margin of long bones. *Blood:* Hemoglobin 80 per cent; R.B.C. 4,340,000; W.B.C. 21,900; Polymorphonuclears 67 per cent. *Urine:* Negative.

Comment.—Whole cow's milk was given during the first six months and this patient received small amounts of cod liver oil and orange juice. Skimmed milk was given from the sixth to the ninth month. Vomiting had been a prominent feature during the first six months of life. It is possible that vomiting might have initiated the process even though the diet otherwise, with the exception of the elimination of a small amount of fat from the "Vitamin milk" for a short time, was sufficient. Examination did not suggest vitamin A deficiency disease.

Necropsy.—The immediate cause of death was bronchopneumonia with bronchitis, peribronchitis, bronchiectatic abscesses, and fibrinous pleuritis.

Keratinizing metaplasia was found involving the whole of the trachea and many bronchi; also in the ducts of glands of the larynx, pharynx, and tongue. In the renal pelvis there was early metaplasia.

Fat throughout the body showed microscopic evidences of resorption. There was a slight hemosiderin deposit in the spleen; but none in the liver which showed an extreme degree of fat storage.

The pancreas showed a single small duct with metaplasia. The organ as a whole was greatly atrophied and fibrosed, and ducts and acini were filled with inspissated secretions.

CASE 8.—Infant No. 17,323; Necropsy No. A-31-159. The patient, a twelve-week-old infant, was admitted to the hospital on account of a cough of four weeks' duration. Birth weight: 8 pounds 3½ ounces. Admission weight: 10 pounds 12 ounces. Weight-height ratio 0.43 as contrasted with 0.57, the normal for this age. Temperature: 98.8° F.

Diet: For the first three weeks of life, the baby was breast fed, but as the quantity of milk appeared insufficient, the infant was weaned and a formula of whole milk and Karo syrup prescribed. He had been offered from 10 to 12 oz. of whole milk each day, but usually regurgitated a small amount after each feeding. Cod liver oil and orange juice in unstated amounts had been given for some time preceding admission.

Examination: The infant was well developed and nourished and did not appear acutely ill. There was a brassy cough and wheezy asthmatic breathing. Auscultation of the chest showed good aeration with dry and musical râles on inspiration. The eyes were normal.

Roentgenogram: Considerable amount of peribronchial infiltration very dense, and involving both lungs. The lung fields appeared emphysematous. Increased density of metaphyseal margin of long bones. *Blood:* Hemoglobin 80 per cent; R.B.C. 3,960,000; W.B.C. 16,800; Polymorphonuclears 67 per cent. *Urine:* Negative.

Comment.—The diet which this patient received seems adequate, although the quantity of whole milk is rather small for the weight. The onset of the illness was a respiratory infection with terminal bronchopneumonia. No external signs of vitamin A deficiency were observed.

Necropsy.—The immediate cause of death was bronchopneumonia accompanied by, and presumably secondary to, bronchitis and peribronchitis. There were many bronchiectases and numerous bronchiectatic abscesses, and a right-sided empyema secondary to an abscess of bronchiectatic origin.

Keratinizing metaplasia was found in the trachea, primary bronchi, and in many small bronchi; also in ducts of tracheal, bronchial, and pharyngeal glands. There was marked hemosiderosis in the spleen and a small amount in the liver. Fat tissue from all locations showed microscopic evidences of resorption.

CASE 9.—Infant No. 17,344; Necropsy No. A-32-32.—This infant, eight months of age, was admitted to the hospital on account of eczema, diarrhea, and failure

to gain. Birth weight: 8 pounds 4 ounces. Admission weight: 11 pounds 14½ ounces. Weight-height ratio was 0.43 as compared with 0.57, the estimated normal for this age.

Diet: During the first eight months, she received eleven different forms of feeding. Breast milk had never been given. Whole cow's milk, goat's milk, evaporated milk, "vitamin" milk, etc., had been given for varying periods in an effort to control the eczema and to control a rather persistent diarrhea. One teaspoonful of cod liver oil and one ounce of orange juice had been given daily since the baby was three months of age.

Examination revealed a poorly nourished and developed, white female infant with a severe form of eczema, and a moderately severe respiratory infection. During the following four months of hospitalization, the patient had recurrent attacks of suppurative otitis media which necessitated bilateral mastoidectomy. Furunculosis was a frequent complication. Finally her condition improved and she was discharged home only to be readmitted at the end of two weeks in a state of collapse which proved fatal. The eyes were normal.

Roentgenogram: Peribronchial infiltration involving both lungs. No localized consolidation. *Blood:* Hemoglobin 65 per cent; R.B.C. 4,000,000; W.B.C. 11,300; Polymorphonuclears 24 per cent; Leucocytes 72 per cent. *Urine:* negative.

Comment.—Although this patient had received many formulas still in the main, they contained presumably optimal amounts of vitamin A and during the periods of hospitalization (four and one-half months) she received an adequate diet. It is possible that the rather persistent diarrhea limited proper utilization of an adequate amount of vitamin A. The severe furunculosis was assumed to be related to the general sepsis and was not taken as a sign suggestive of avitaminosis. Other external signs were not recognized.

Necropsy.—No satisfactory anatomic cause of death was found. The lungs showed only a slight bronchitis. Occasional alveolar ducts were filled with connective tissue, the result of organization of exudate. There were numerous groups of atelectatic alveoli mostly filled with mononuclear cells.

The evidences of vitamin A deficiency were few and apparently of recent origin. In the trachea there was extensive early metaplasia, atrophic ciliated cells undermined by stratified cells reproducing accurately the early stage of metaplasia as seen in experimental animals. Likewise, in the pelvis of the kidney there was early metaplasia.

Fat tissue from subcutaneous tissue, mesentery, mediastinum, and regions of adrenals and kidneys showed also complete loss of fat with reversion to the embryonic state.

Sections of the vertebra and costochondral junctions show almost complete arrestment of growth of bone with atrophy of the zones of proliferating cartilage.

The spleen showed hemosiderosis.

The histology of the skin was that of a chronic dermatitis accompanied by abscesses in the corium.

The history and the postmortem findings indicate clearly that vitamin A deficiency was not the initial cause of this infant's illness. On the contrary, the evidence showed that the deficiency developed late and the inference is warranted that it was a consequence of factors which prevented the utilization of the adequate diet received by the patient.

CASE 10.—Infant No. 17,436; Necropsy No. A-31-189. The patient, a female infant, and a twin sister of Case 13, was admitted to the hospital when seven months old, because of failure to gain, a cough since birth, and recurring attacks of fever associated with pyuria. Vomiting and diarrhea were not conspicuous symptoms.

Birth weight: 7 pounds. Weight on admission: 8 pounds 10 ounces. Weight-height ratio 0.37 as compared to 0.64, the normal for this age. Temperature: 101.4° F.

Diet: The baby was breast fed for two days only and then given lactogen and water. The infant did not gain, so when two months old the food was changed to skimmed milk with added carbohydrate, a diet which had been continued until the time of admission. Cooked cereal was added at four months of age. Cod liver oil had not been given.

Examination showed a very poorly nourished and developed female infant with bilateral conjunctivitis, bilateral keratomalacia, bilateral otitis media, consolidation of the upper lobe of the right lung, and pyuria. The infant did not respond to therapy and died thirteen days after admission.

Fig. 4.—Photomicrograph of section of kidney (Case 10) showing metaplasia of epithelium lining pelvis. Note large amount of keratinized débris in renal pelvis. Hematoxylin and eosin; ×115.

Roentgenogram: A pyramidal dense area involving the apex of the right lung, with cavitation. *Bones:* Increased density of metaphyseal margin of long bones. *Blood:* Hemoglobin 80 per cent; R.B.C. 3,000,000; W.B.C. 26,500; Polymorphonuclears 81 per cent. *Urine:* Albumin was present with large numbers of leucocytes and erythrocytes in clumps.

Comment.—On account of a history that the mother could not tolerate fat, plus the fact that the baby developed a diarrhea on whole milk, a fat-free diet was given this infant for a period of six months. Vitamins were not added. The classical picture of vitamin A deficiency disease was observed on admission. Although there were evidences of renal infection, special studies for keratinized cells were not made.

Necropsy.—The immediate cause of death was bronchopneumonia with bronchitis, peribronchitis, bronchiectases, bronchiectatic abscesses, and organizing fibrinopurulent pleuritis.

Keratinizing metaplasia was found in the mucosa of the nares, trachea, and bronchi of all sizes; in renal pelvis, ureters, periurethral glands; in the fundus of the uterus; in pancreatic and submaxillary gland ducts.

In the respiratory tract and genitourinary tract the replacement of keratinizing stratified epithelium was very extensive.

Fat tissue from all locations showed almost complete absence of fat.

There was very heavy hemosiderin deposit in the spleen both in cells, in the sinuses, and in the reticular tissue of the red pulp. There was a slight deposit of hemosiderin in the liver cells. The marrow of the ribs was atrophic. The costochrondral junctions showed the early reaction of scorbutus.

The pancreas showed marked fibrosis, atrophy of acini, and marked dilatation of ducts and acini with inspissated secretion. Keratinizing metaplasia was evident to a slight degree in a rare duct of small caliber.

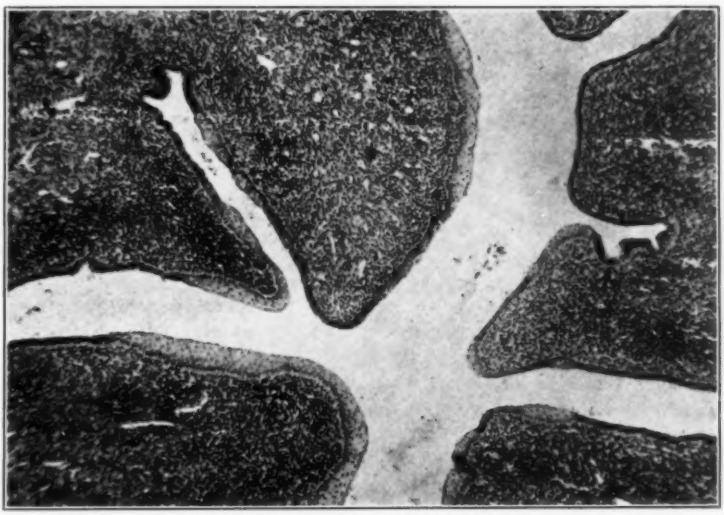

Fig. 5.—Photomicrograph of section of uterus (Case 10). Note stratified squamous epithelium. Hematoxylin and eosin; ×115.

The epithelial changes in the organs of this infant were fully as striking as those in the case reported by Wilson and DuBois; and presented, on the whole, the usual picture found in rats and guinea pigs in experimental vitamin A deficiency.

Case 11.—Infant No. 17,517; Necropsy No. A-32-16. The patient, when five months of age, was admitted to the hospital with icterus which was observed first when she was three weeks old. The stools had always been the color of clay and after voiding, the diaper was stained distinctly yellow. Birth weight: 8 pounds. Admission weight: 9 pounds 10 ounces. Weight-height ratio was 0.23 as compared with 0.60, the normal for the age.

Diet: She was breast fed for two weeks and then given a formula of whole cow's milk with added carbohydrates. Viosterol and orange juice had been given twice daily since one month of age.

Examination revealed a poorly nourished and developed female infant with jaundice and bilateral otitis media. There was generalized adenopathy and both

the liver and spleen were palpable. Eyes were normal. The stools were clay-colored. The urine contained a large trace of bile. Icteric index: 125. Direct van den Bergh: 49.50 units. The diagnosis of congenital obliteration of the bile ducts was confirmed by exploratory laparotomy. The patient died a few days later.

Roentgenogram showed slight peribronchial thickening. *Blood:* Hemoglobin 65 per cent; R.B.C. 3,670,000; W.B.C. 15,750; Polymorphonuclears 45 per cent. *Urine:* Albumin +; bile +++; occasional leucocytes and granular casts.

Comment.—In this case, there were no external evidences suggesting deficiency disease and the abnormal findings in the urine were not considered as being of importance. The total consumption of a food high in vitamins would seem to have excluded a dietary deficiency.

Necropsy.—The immediate cause of death was peritonitis and bronchopneumonia. The primary cause was complete congenital atresia of the common bile duct.

The bronchopneumonia was acute, not accompanied by peribronchitis or interstitial invasion of the lung. The liver showed bile stasis in bile ducts and bile capillaries, there was marked increase of fibrous tissue and bile duct proliferation in, and adjacent to, the portal spaces. In many lobules there was increase of connective tissue about the central (hepatic) vein.

Keratinizing metaplasia was found in the trachea, ducts of the glands of the esophagus, and in the pelvis of the kidneys. In the portion of the trachea examined, at the level of the lower pole of the thyroid, the normal epithelium was completely replaced by a stratified squamous keratinizing epithelium. In the renal pelvis also the metaplasia was complete and there were large masses of accumulated desquamated keratinized cells.

The epithelium of the esophagus was markedly hyperplastic with a thick adherent layer of keratinized cells. Ducts of esophageal glands were lined with stratified squamous epithelium.

The thymus, as is the rule, was very atrophic. The Hassall corpuscles were greatly enlarged, some being 2 mm. in diameter. They consisted of cavities lined by shallow stratified squamous epithelium and filled with closely packed flat keratinized cells. This enlargement of Hassall's corpuscles has been noted in rats and guinea pigs in vitamin A deficiency.

Fat tissue from all locations showed microscopic evidence of fat resorption. The spleen contained a small amount of hemosiderin in phagocytic cells.

Sections of two parathyroid glands showed an unusual picture not seen in any of the other cases of this series, nor in rats and guinea pigs in experimental vitamin A deficiency. The blood vessels of both glands were greatly engorged and both glands contained many large cavernous spaces lined with endothelium and filled with blood. There was a considerable fibrosis throughout both. The parathyroid cells, though reduced in number, appeared to be normal. At the periphery of each gland, there was a narrow zone without parathyroid cells, consisting of vascular blood-filled spaces and fibrous tissue. This zone contained many phagocytic cells filled with hemosiderin granules.

CASE 12.—Infant No. 19,260. The infant, a male, aged six and one-half months, was admitted to the hospital because of drowsiness of four days' duration. He was a fairly well-developed and well-nourished white male infant, quite apathetic and obviously acutely ill. Weight: 13 pounds 6 ounces.

Diet: The patient was breast fed for eight days only and then was given cow's milk. On account of the appearance of allergic manifestations at this time he was

given a Sobee formula, a formula that was used until the time of admission. Viosterol had been given but orange juice and cod liver oil had never been supplied.

Examination: Both eyes showed advanced keratomalacia. The neck was retracted and the sutures of the skull showed some separation; there was also a bilateral otitis media. Urinalysis showed numerous white cells with occasional red cells and a large number of epithelial cells. Spinal fluid was normal.

Roentgenogram: Slight amount of peribronchial thickening.

Bones: Increased density of metaphyseal margin of long bones.

Blood: Hemoglobin 80 per cent; R.B.C. 600,000; W.B.C. 14,000; polymorphonuclears 63 per cent.

Urine: Albumin, erythrocytes, leucocytes, and a few epithelial cells.

Comment.—Without much doubt, vitamin A deficiency disease was initiated as the direct result of an inadequacy of vitamin A in the diet. In addition to the diagnostic sign, keratomalacia, epithelial cells were present in the urine in unusual numbers. The activity of the process in the eye subsided under therapy but with blindness as a resultant effect.

CASE 13.—This patient, aged four months, was the twin sister of Case 10. She was admitted to another hospital June 8, 1929 and died there June 18, 1929. A routine postmortem was done by the pathologist, and we have had opportunity to read the protocol and to study the histologic preparations.

Diet: The diet, practically since birth, had consisted of skimmed milk with added carbohydrates. Cooked cereals were added early. Cod liver oil had not been given.

Comment.—At three months of age her weight was six pounds. She entered the hospital because of failure to gain, and cough. Her respirations were described as asthmatic in type. Several formulas were tried, among them a fat-free milk diet. She died with evidences of extensive pulmonary consolidation, with a tentative diagnosis of tuberculosis.

Necropsy.—The immediate cause of death was bronchopneumonia with chronic bronchitis, peribronchitis, and bronchiectatic abscesses.

There were no sections of trachea and renal pelvis; however, keratinizing metaplasia was found in the bronchi. There were early foci of metaplasia in the body of the uterus. The liver contained much hemosiderin in hepatic cells and in phagocytic cells of the sinusoids. The spleen was of the atrophic type with considerable hemosiderin in phagocytic cells in pulp, cords, and sinuses.

Fat tissue in all locations showed extreme fat resorption and the lobules had reverted to embryonic appearance.

The pancreas showed atrophy, fibrosis, and great dilatation of acini and ducts with inspissated secretion.

Diet.—As mentioned previously, the development of vitamin A disease is linked closely with the adequacy or inadequacy of vitamin A and presumably carotin in the food consumed and the amount available for use in the body tissues. Therefore, the cause of the disturbance in this series of cases should be found by an analysis of the dietary history or by the presence of some factor or factors interfering with the utilization of this essential substance.

In six infants with keratomalacia, according to the dietary history, two patients (Cases 1 and 4) had received condensed milk exclusively for about four months before admission to the hospital; two patients (Cases 10 and 13) had been fed formulas of skimmed and fat-free milk

for five months; one patient (Case 12) had received various low fat and protein milk mixtures and Sobee over a period of about six months; and one patient (Case 5) although offered a mixture of whole milk, water and dextrimaltose was unable, on account of a congenital anomaly, to swallow or retain a sufficient amount for preventive needs. Cod liver oil or orange juice had never been given to these patients. Therefore, in these infants, it is reasonable to assume that primarily the histologic and clinical manifestations were the result of an inadequacy of vitamin A in the diet.

An analysis of the dietary histories of 7 patients who did not present recognizable clinical signs of the disease during life *failed* to reveal an inadequacy of vitamin A in the diet, prior to the time of admission to the hospital. As determined from the history, 6 patients had received cow's milk in dilution, adequate in calories and affording from one and a half ounces to three ounces of cow's milk per pound of body weight. Also they had received cod liver oil and orange juice. Furthermore, 4 patients received cod liver oil and orange juice with cow's milk dilution for a considerable period of time while in the hospital. Possibly in one patient (Case 2) who had been breast fed exclusively since birth, the histologic findings might be related to the inadequacy in the diet, as it is known that the Vitamin A content of woman's milk varies widely in certain instances. Inasmuch as at least 6 of these patients had received an amount of vitamin A usually regarded as being protective for young infants, the development of the histologic changes was probably a consequence of grave metabolic disturbances interfering with proper absorption, storage, and utilization of vitamin A or its precursor, carotin. In this series, the factors held responsible were chronic generalized infection in five instances, if the breast-fed infant is excepted, and congenital obliteration of the bile ducts in one instance. Extensive chronic sclerosis of the pancreas with dilatation of the ducts was found in 3 of the patients with pulmonary infection who apparently had been receiving an adequate amount of vitamin A, as well as in 3 patients who had not been receiving an adequate amount of vitamin A in their diet. What part this pathologic process plays in bringing about the characteristic changes in the epithelial cells by inhibiting complete cleavage of fats cannot be stated at this time, particularly as such changes are not an uncommon finding in infants, unassociated with histologic evidences of vitamin A deficiency. Among other writers Higgins and Mallory,[17] in a recent report, refer to a patient with keratomalacia, in whom there was a congenital anomaly of the gall bladder and sclerosis of, and dilatation of, the ducts of the pancreas. In this patient only 40 per cent of the ingested fat was absorbed and 70 per cent was in the form of neutral fat. Further confirmatory evidences of the effect of disturbances of fat metabolism have been reported.[15, 18]

TABLE I

PERCENTILE ESTIMATED INDEX OF UNDERNUTRITION DETERMINED BY A COMPARISON OF AGE AND WEIGHT ON THE BASIS OF THE EXPECTED NORMAL WEIGHT FOR THE AGE

CASE NO.	AGE MO.	SEX	CASE WT.	NORMAL WT. FOR AGE	PER CENT UNDERWEIGHT
1	5	F	6.5	15.3	58
2	1	M	6.8	10.2	33
3	4½	M	5.0	15.6	68
4	3½	M	5.4	10.6	51
5	5½	M	6.3	16.7	62
6	18	M	16.0	24.5	34
7	9	M	11.8	19.5	39
8	3	M	10.8	13.7	21
9	8	F	11.9	17.7	33
10	7	F	8.6	17.0	49
11	5	F	9.6	15.3	37
12	6½	M	13.4	17.7	24
13	7	F	Died at home. Necropsy.		

As to the concomitant features of this disease, inanition and stoppage of growth, infection and lesions of the eye, they paralleled closely in frequency and severity, the features observed when the disease is induced experimentally in animals and in general, with the cases reported in the literature heretofore.

Inanition and Cessation of Growth.—The state of nutrition was estimated by comparing the age and weight on admission with the expected average normal weight for the age. These figures are given in Table I. The percentile degree of undernutrition was from 20 to 40 in seven patients, 40 to 60 in three patients, and 62 and 68 in two patients. The weight of one patient was not available as she died at home (Case 13).

For the purpose of contrasting the degree of undernutrition with the degree of arrest in growth, the length of the body was compared with

TABLE II

A COMPARISON BETWEEN THE WEIGHT-HEIGHT RATIO AS ESTIMATED AND THE EXPECTED NORMAL WEIGHT-HEIGHT RATIO FOR THE AGE

CASE NO.	CASE HT.	NORMAL HT. FOR AGE	CASE WT./HT. RATIO	NORMAL WT./HT. RATIO
1	22.8	25.3	0.28	0.60
2	21.6	21.9	0.31	0.47
3	22.8	25.3	0.22	0.62
4	19.6	24.0	0.28	0.47
6	29.6	31.9	0.54	0.77
7	25.2	28.1	0.47	0.69
8	25.2	24.1	0.43	0.57
9	24.8	27.1	0.48	0.65
10	23.2	26.6	0.37	0.64
11	24.4	25.3	0.39	0.60

the expected average normal length for the age. These figures, given in Table II, show that the measurements secured after death, fell well below the estimated average normal length for the age in 9 patients.

In one patient, who was 21 per cent underweight (Case 8), there was a slight increase in length above the average normal for the age. The length of one patient (Case 2) was practically identical with the average normal for the age. A comparison between the weight-height ratio with the estimated average normal weight-height ratio for the age indicates an index well below the estimated normal in all of the patients (Table II).

Observations with reference to stoppage of growth of the long bones were also made with the aid of the roentgen ray. Definite evidences of cessation, or at least retardation, of growth were present in 5 patients, as indicated by a band of moderately increased density of the metaphyseal margin. Equivocal findings were present in 5 patients. One of these patients showed osteoporosis. Roentgenologic changes indicative of mild or healed rickets were not present in any of 10 patients examined. In one patient (Case 1) microscopic examination of the ribs showed very early changes indicative of scurvy.[20]

The degrees of undernutrition and retardation in bone growth were not related to the appearance of eye lesions or to the extent of histologic changes found at necropsy. Just how variable these features may be is illustrated by the following cases. In Case 4 with keratomalacia the degree of undernutrition was 51 per cent and involvement of one site was demonstrated histologically (bronchi), whereas in Case 10 with keratomalacia in which the degree of undernutrition was estimated as 49 per cent, there was involvement of seven sites (nasal mucosa, bronchi, salivary glands, pancreas, ureter, kidney pelvis, and uterus). Eye lesions were present in the patient (Case 5) with an index of 62 per cent underweight, but absent in the patient whose index was 68 per cent underweight. On the other hand, the patient (Case 3) who was 68 per cent underweight and in whom three sites (bronchi, salivary glands, and pancreas) were involved, did not develop eye lesions.

That retardation of growth goes hand in hand with the disturbances of nutrition is implied by the weight-length data and the findings in the roentgenograms. In fact, there appears to be a somewhat more orderly proportion between length and weight in this disease than is customarily seen in the dietary diseases following a deficiency of vitamins C and D. Nevertheless, undernutrition and retardation of growth, unlike the situation in the experimental production of this disease, cannot be taken as a safe criterion of vitamin A deficiency disease in infants, inasmuch as the qualitative inadequacy of the diet is but one of the many causative factors bringing about failure to grow and loss in weight.

Infection.—Infection, especially of the respiratory tract as indicated by the objective symptom "cough," was the chief reason for bringing 5 of the patients to the hospital. Failure to gain, anorexia,

vomiting, diarrhea, together with fever and cyanosis, and labored breathing, were additional symptoms. One patient was admitted with chronic eczema and pansinusitis, and in one patient, jaundice had persisted since birth. One patient was admitted on account of "conjunctivitis." He was allergic to cow's milk and the lesion of the eye was noticed shortly after "bloody urine" appeared. One patient was brought on account of failure to gain. The duration of respiratory infection before admission to the hospital, as estimated in 7 patients by the time of onset of symptoms in the history, was as follows: One month in 4 cases, about three months in 2 cases, since birth in 1 case.

Physical signs of a diffuse infiltration of the lungs were revealed by examination at the time of admission in 5 instances. A terminal bronchopneumonia developed in 6 of the remaining patients. Involvement of the respiratory system as confirmed by roentgenograms in 9 patients consisted of generalized infiltration of the lungs; in 8 of these there were unmistakable evidences of emphysema. One patient exhibited a sizable area of consolidation, and an area of consolidation with cavitation was demonstrated in another patient.

It should be reemphasized that in all of the 11 patients studied at necropsy, histologic changes were detected in one or more parts of the respiratory system. Metaplasia of the epithelium was demonstrated in the trachea alone in 4 cases, in the bronchi alone in 2 cases; associated lesions were found in the trachea and bronchi in 5 cases and in the nasal mucosa and bronchi in one case. But when it came to correlating the lesions with the onset, duration, or severity of the respiratory symptoms, such widely divergent results were obtained that no conclusions could be drawn as to whether the alteration in the epithelial cells was primary to the onset of the infection or whether infection developed primarily.

It must be remembered that the histologic changes described are those encountered in the study of tissue selected in the course of routine postmortems. More extended microscopic studies would undoubtedly have revealed keratinizing metaplasia in other situations. However, in discussion of the relationship between infection and condition of the respiratory mucosa in vitamin A deficiency, we repeat that the epithelium is functionally severely affected long before it is replaced by the stratified keratinized epithelium. In vitamin A deficiency there is a progressive atrophy terminating in a nonviable epithelium which becomes replaced by the keratinizing epithelium through reparative proliferation of basal cells.

One observation may be cited which possibly throws some light on this question.

A white male infant (Case 4), three and one-half months old, had been fed exclusively on boiled condensed milk and water without cod liver oil or orange juice. One month prior to admission, he developed signs of a severe "respiratory

infection," the formula was refused, and he vomited whenever it was forced. Physical examination revealed an emaciated infant with labored breathing, cyanosis, and consonating râles throughout both lungs. Both eyes showed keratomalacia. He weighed 5 pounds 4 ounces, the temperature was normal, and the white blood cells were 39,000 per cu. mm. The differential count was normal. Roentgenograms showed evidences consistent with a *lobular pneumonia*. The roentgenologist stated, "The films of the chest show a diffuse, quite dense pneumonic infiltration, generalized in distribution, but most marked in the midportions and in the upper right lobe." Prompt institution of a high vitamin A diet with cod liver oil and orange juice was followed by a remarkable improvement of the lesions in the eyes and, after ten days, a steady gain in weight, throughout which period the temperature was within normal levels. With the gain in weight, the physical signs gradually disappeared from the lungs and a roentgenogram, at this time, was reported as follows: "Re-examination of the chest still shows a considerable amount of quite dense infiltration in the midportions although there has been definite clearing since the previous film." He gained about one pound in twenty-seven days and improved steadily until suddenly the temperature became elevated, signs of activity appeared in the lungs, and he lost weight. Death ensued five days later. Necropsy showed bronchitis, peribronchitis, bronchopneumonia (organizing), interstitial emphysema, and bronchiectatic abscesses. Keratinization of the epithelial cells was demonstrated in the trachea and bronchi. In reconstructing the sequence of events, it would seem that as a consequence of a diet low in vitamin A there was loss in weight, nutritional failure, keratomalacia, and the development of atrophy and cornification of the epithelial cells occluding the bronchi. Resolution followed the administration of vitamin A, as shown by improvement of the eyes, gain in weight, and disappearance of the signs in the lungs; but then, as has happened so often in our experience with dietary deficiency diseases, death resulted from a secondary or terminal bronchopneumonia. The postmortem studies support this interpretation, because we were able to recognize, in addition to persistent metaplasia in some locations, stages of repair in the return of epithelium to the physiologically normal type. This experience is instructive and suggests that clinical and roentgenologic signs of respiratory disease may be initiated primarily by the atrophy and possible metaplasia of the mucosa of the respiratory tract and, because of the lowered resistance of the epithelium, infection follows secondarily. Whether this is the regular sequence of events in all cases cannot, of course, be stated from a single observation.

Urine.—An abnormal number of formed elements in the urine were noted in the records of 3 patients (Cases 10, 11, and 12). In one patient (Case 10) many red and white cells and granular casts were found and microscopically keratinized epithelial cells were demonstrated in the ureters and kidney pelves. Urinalysis of the patient who recovered (Case 12) showed in addition to red and white cells many epithelial cells. Special attention, however, until recently has not been paid to the significance of epithelial cells in the urine. It is important to note that changes were found in the kidney in 4 of the cases studied histologically (Cases 1, 9, 10, 11) and, therefore, it is not unlikely that with more diligent search, a large percentage of cases might have revealed these elements so characteristic of a lack of vitamin A.

Skin.—As might be expected, dehydration with dryness of the skin was apparent in many of the patients with high fever, active signs of infection, and undernutrition. Infection of the skin, localized or general, was noticeable by its infrequency in these cases. The question is raised, especially in the absence of characteristic histologic changes in the structures of the skin, as to the diagnostic importance of xerosis of the skin and skin infections. When these signs do occur, are they not due more directly to dehydration, undernutrition, and coexisting generalized infection?

Eyes.—In connection with the visual disturbances which are frequently associated with A avitaminosis, it is obvious that night-blindness can be recognized in small infants only with difficulty if at all. Keratomalacia occurred in 6 patients and according to the dietary history, each patient had received a subminimal amount of vitamin A for a long time before its appearance (Cases 1, 4, 5, 10, 12, 13). Two of the patients (Cases 1 and 4) had been fed condensed milk about four and three and one-half months, respectively, before eye signs appeared. One patient (Case 5) although being offered a mixture of whole milk, water, and dextrimaltose had never been able to swallow or retain an amount sufficient for preventive needs and developed this symptom when five months old. Keratomalacia appeared in 2 patients (Cases 10 and 13) after five months on formulas of skimmed and fat-free milk. The sixth patient (Case 12) who was allergic to cow's milk had received a variety of low fat and protein food products, including Sobee, for nearly six months before the eye signs were observed. *Cod liver oil had never been given to the six patients with keratomalacia.* In all patients, undernutrition preceded the onset of the lesion of the eyes. However, so constant a correlation could not be established between infection or the extent of the sites involved histologically. Respiratory infection followed the development of keratomalacia in 3 patients (Cases 4, 5, and 10). In one patient (Case 1) four sites were involved (bronchi, salivary glands, pancreas, and uterus); in another patient (Case 10) keratinization of the epithelial cells was found in seven different locations (nasal mucosa, bronchi, salivary glands, pancreas, ureter, kidney pelvis, and uterus). On the other hand, in 2 other patients with keratomalacia who were examined after death, only the trachea and bronchi were involved in one patient (Case 4) and, in the other patient (Case 13), only the bronchi, uterus, and pancreas showed the epithelial changes indicative of a lack of vitamin A. The percentage incidence of keratomalacia (40 per cent) in this series of cases agrees with the lack of correlation of the condition of the eyes and other manifestations when the disease is induced in experimental animals. Furthermore, it confirms the fact that keratomalacia is a *late sign* of vitamin A deficiency.

TABLE III

CLINICAL AND PATHOLOGIC SUMMARY OF REPORTED CASES

CASE	AGE (IN MONTHS)	SEX	DIET VITAMIN A		CLINICAL MANIFESTATIONS			URINE (ALBUMEN R.B.C., W.B.C.)	CLINICAL DIAGNOSIS	RESULT
			ADEQUATE	INADEQUATE	PERCENTAGE UNDER-WEIGHT	KERATOMA	RESPIRATORY INFECTION			
1	5	F		+	58	+	+		A deficiency pneumonia	Died
2	1	M	+		33		+		Pneumonia	Died
3	4½	M	+		68		+		Pneumonia	Died
4	3½	M		+	51	+	+		Pneumonia a deficiency	Died
5	5½	M		+	62	+	+		Anomaly of C.N.S. and G.I. tract a deficiency	Died
6	18	M	+		34		+		Pneumonia	Died
7	9	M	+		39		+		Pneumonia	Died
8	3	M	+		21		+		Pneumonia	Died
9	8	F	+		33		+		Eczema pansinusitis pneumonia	Died
10	7	F		+	49	+	+	+	A deficiency pneumonia	Died
11	5	F	+		37		+	+	Congenital obliteration of bile ducts	Died
12	6½	M		+	24	+		Epithelial cells	Pneumonia a deficiency	Improved
13	4	F		+	?	+	+			

Early Signs.—Increasing attention is being focused on the early signs indicative of vitamin A deficiency disease. Thatcher and Sure, who have confirmed the observations of Wolbach and Howe, state "that histological changes may develop in tissues before any external symptoms are apparent." Evans[19] demonstrated the appearance of cornified cells in the vaginal secretions of rats and believed this to be the earliest sign and found in no other deficiency disease. Both Bloch[15] and Spence[21] believe that in children urinary infection as well as dryness of skin and skin sepsis are frequent and important accompaniments of the condition.

But as mentioned, significant clinical and histologic features appear with such *irregularity* and *inconstancy* as to render the diagnosis before the development of keratomalacia exceedingly difficult. Nevertheless a correlation of the clinical and histologic data in this series of patients and the experience of laboratory workers and clinicians, reveal that certain diagnostic criteria stand out prominently which, when they occur, singly or in combination, should lead one to infer that an optimum amount of vitamin A, either from the diet or as the result of an underlying metabolic disturbance, is not available for the maintenance of health.

In connection with the early detection of signs of A avitaminoses, the points for special consideration are (1) analysis of the history in order to determine the adequacy or inadequacy of vitamin A and its precursor, carotin, in the diet; (2) the exclusion of vomiting and diarrhea and of other morbid processes interfering with the metabolism of fats, especially such as chronic generalized infections and diseases of the liver, gall bladder, and pancreas; (3) the appearance of night-blindness and xerosis of the cornea with opaque white deposits on the scleral conjunctiva (Bitot's spots); (4) the demonstration of keratinized epithelial cells in the scrapings from the cornea, the nose, and the mouth, and of secretions from the trachea, bronchi, kidneys, and vagina should serve as confirmatory diagnostic evidence in suspected cases of vitamin A deficiency disease.* In this series of cases, histologic evidences characteristic of vitamin disease were found in the mouth and nose, the trachea and bronchi, the renal pelvis and ureters, and the vagina and uterus.

CONCLUSIONS

In conclusion it may be said that (1) vitamin A deficiency in infants is not altogether infrequent and should be suspected without regard to the absence of the characteristic eye signs. (2) Histologic evidences

*"By far the best differential stain is obtained by the use of the Gram method, with decolorization by acid alcohol. The cornified cells are blue and all the other tissue elements are decolorized. This method is particularly recommended by Schmorl,[23] and we have found it useful in doubtful cases. The cornified cells stain dark brown to black by Levaditi's stain for spirochetes and deep red by Mallory's aniline blue stain." (Farber and Sweet.[22])

of A avitaminosis may occur in infants who are receiving an amount of vitamin A in their diet usually accepted as meeting the minimal protective needs of the body. (3) The explanation offered is that some factor or factors interfering with the storage or utilization of this vitamin lessen the availability of the supply essential for normal nutrition. (4) Certain diagnostic criteria are suggested whereby it should be possible to establish the diagnosis in the early stage. (5) Vitamin A deficiency disease should be considered as a general systemic disease rather than as a local disease of the eye.

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PROLAPSE OF THE RECTUM IN CHILDREN

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THE treatment of prolapse of the rectum in children is confused at present in the mind of the practitioner. This is no doubt the result of the trend in the literature on this subject since 1910. The surgeon, too, frequently resorts to needless operative procedure in cases in which simple training and carefully followed out toilet routine would usually suffice. Since the publication of an article on this subject in 1926, and as the result of a larger experience, I am more firmly convinced that, with rare exceptions, the majority of cases respond readily to the simple treatment detailed later.

The publications of Lockhart-Mummery in 1907 and 1913, on prolapse of the rectum in children, still remain the classical references on this subject and have been quoted in all subsequent writings. The articles were based on the study and treatment of 50 cases of rectal prolapse occurring in the Children's Service of Northeast London Hospital. An etiologic division was made as follows: 14 of his cases of prolapse followed diarrhea; 13, adenoids; 3, worms; 3, rectal polypi; and 3 followed whooping cough. For 16 there was no ascertainable cause. Lockhart-Mummery further calls attention to two anatomic and physical conditions that may have a decided bearing upon the increase of rectal prolapse. In the first place, he points out that the rectal support in the infant is largely fat and that any condition or wasting disease that tends to break down this fat lowers normal rectal support, making the patient more susceptible to prolapse. This viewpoint has not been wholly accepted, as prolapse is very often seen in the well-nourished child. On the other hand, certain German writers have called to our attention the fact that during the late years of the war and for two years following, when a definite food shortage was known to exist throughout the Central Empires, rectal prolapse was seen far more frequently in children's clinics. The second and physiologic cause is the assumption of an unnatural position of defecation as contrasted with the normal squatting position. In the adult, the rectum is distinctly angulated to meet the sacrococcygeal curve, whereas in the child the anterior curvature of the coccyx is not fully completed. The rectum is consequently straightened out without the normal angulation to break the force of the fecal current. Furthermore, the pelvic organs are comparatively high in the pelvis of the child, and such normal support as may be gained from the proximity of the organs is lost.

The infant is early trained in a false posture for defecation. The present-day stool is built so high that the feet cannot possibly rest upon the floor. The child is taught to sit in an upright position. The pelvic fascia is thus relaxed and the coccyx is not drawn forward, as is intended. The result is that the straightness of the rectal tube is accentuated. Again, in this abnormal position, the intraabdominal pressure and splinting of the abdominal muscles from pressure by the thighs, is completely lost. The adult-sized toilet seat was not mentioned by Lockhart-Mummery as an additional contributing factor. It furnishes no support to the infant, but tends to overspread the buttocks and thus lose this final support to the rectum.

Lockhart-Mummery calls attention to the fact that prolapse of the rectum is little known among primitive people and is scarcely ever seen in animals. The primitive man from earliest childhood assumes the low squatting posture and thereby avoids rectal strain. In summing up the treatment, he calls our attention to the tendency to outgrow the prolapse by the sixth or seventh year. Prolapse frequently disappears following rest in bed. Six patients in his group were treated surgically. The operative procedure consisted of linear scarring and multiple ligations. Since the publication of this article, nearly all writings have had to do with the various types of operative technic and reported results. The more radical procedures are used in the German and Austrian clinics. Unfortunately, these radical procedures have been copied and recopied, in both European and American textbooks, with such regularity that there is little wonder that the treatment of this condition has taken on such a serious aspect. The reports of mortality, as well as of recurrences, place all of these major operative procedures in a very questionable status. Several technics have been devised for reduction in the size of the anal aperture or the shortening of the sphincter muscle. These are:

First, plastic operations upon the external sphincter with an attempt to shorten the muscle.

Second, the introduction of nonabsorbable suture material.

Third, the reduction of the anal orifice by surrounding the rectum at the external sphincter with a band of free transplanted fascia.

Fourth, and possibly the most vicious of all procedures for the reduction of the anal lumen, is the introduction of a subcutaneous ring of silver or phosphorbronze wire. The surgeons advocating these methods curiously comment on the unfortunate fact that fistulas and suppuration occur too frequently as a result of the last named procedure. It has been reported that series of such cases number as high as fifteen or twenty in a single clinic.

In 1919, Leonard Findlay, while visiting in Geneva, learned of a new method in the treatment of prolapse of the rectum in children, as practiced by Professor D'Espine. The technic consisted of the

injection of alcohol in the perirectal spaces. Previously, ergot, carbolic acid, white oak bark, and various combinations of alcohol and glycerine, as well as other chemicals, had been injected in the perirectal spaces with the idea of producing low grade inflammatory reaction and subsequent fibrous tissue formation, for the purpose of giving support and fixation to the rectal wall. In 1921, Findlay reported 21 cases, and again in 1923, 41 patients having rectal prolapse, on all of whom successful cures were effected by the D'Espine method. Since this time, sizable series have been reported by Alexander, of Philadelphia, Brown and Drake, of Toronto, and Fraser, of England.

The technic in this method is comparatively simple. A general anesthesia is required. The perineum is prepared and the knees are flexed on the abdomen. An ordinary exploring syringe filled with 95 per cent alcohol, and a fine calibered needle at least two and a half inches in length, are used in the procedure. If the prolapse occurs as a result of straining with the anesthesia, it is replaced, the index finger of the left hand being inserted into the rectum as a guide. The needle is introduced on each side, one-fourth of an inch from the anal margin, and 1.5 c.c. of 95 per cent alcohol is injected just outside the rectal wall at a depth varying from 1 to 1½ or 2 inches. The subsequent care consists of strapping the buttocks, placing the child in bed for ten days, and having him perform all bowel movements in the horizontal position. Although this method was successfully used on one patient at the Saint Louis Children's Hospital in 1925, it has not since been repeated, nonoperative methods having proved successful.

TYPES OF PROLAPSE

Prolapse of the rectum as seen in children, rarely involves more than a mucous membrane, and appears only during the act of defecation, severe paroxysms of coughing, excited laughter, violent exercise, or injuries. It is inclined to retract immediately. If the prolapse is progressive, the tendency is gradually to force down more mucous membrane, and the return of the mass is increasingly retarded. In a later stage, the prolapse remains outside the rectum unless replaced manually. The early appearance is merely that of protruding folds of mucous membrane with the mucocutaneous line and its pilebearing area forced into view. At this stage some confusion may exist in a differential diagnosis between prolapsed mucous membrane and hemorrhoids. The difference, however, is quite readily made; first, on the general assumption that hemorrhoids are a rarity in childhood, second, that the protrusion appears in circling folds of smooth mucosa, whereas hemorrhoids are distinctly lobulated and spring from the mucocutaneous line. Bleeding is of no aid in this differential diagnosis since it occurs in both conditions. Prolapse of the rectum involving all coats of the bowel, presents a different picture, in that the prolapse is larger

both in diameter and in length, and shows a definite sulcus at the anal margin since the mucocutaneous line is not forced down as in the simple mucosal prolapse. The generally recognized third degree prolapse is one of invagination or intussusception. The invagination may take place at the rectosigmoid junction or at an anatomic weak point of suspension of the sigmoid or rectum. Obviously, this type does not represent the simple prolapse seen in children and here a surgical procedure alone will effect a cure. This is not true in the second variety in which all the walls of the rectum are involved, since many of these were of the type seen in our series.

The condition of the sphincter muscle is very significant in estimating the degree of the prolapse and the possibility of the subsequent cure. At this point it is well to mention the fact that children who have had imperforate rectum and anus will have mucosal prolapse, for it is quite obvious that if any sphincter muscle is present it is so fixed in scarred tissue that it fails to function. This is likewise true in the very occasional patient who appears to have no anal canal, and the mucosa apparently meets the true skin in a fixed line. This congenital abnormality subjects the patient to fissures, small marginal ulcers, and a tendency to the prolapsing of the mucosa. The two above conditions are not to be confused with the true prolapse of the mucosa and no amount of strapping or rest in bed will have the slightest effect in improving the condition. Again, in certain cases, the external sphincter appears to be widely placed about the rectal margin and the muscle itself appears abnormally weak in tensing of the perineum and in contraction of the anal outlet. These patients may require prolonged treatment in developing this musculature. The sphincter ani is particularly responsive to stimuli in normal children. At the first attempt at examination the sphincter tightly contracts, and the perineum is tensed and retracted forward. In an advanced case of rectal prolapse in which the protruding mass remains outside the anus, the sphincter is patulent and after the mass is reduced, is contracted only by real effort on the part of the patient. In the remission following the voluntary contraction, the sphincter again becomes patulent. When the examining finger is introduced into the rectum, no resistance is found, and all voluntary attempts at contraction are decidedly weak. Only in neurologic cases in which the nerves are destroyed by tumor or spina bifida is there no response at all. The early condition of mucosal prolapse scarcely affects the sphincter muscle. Directly following the act of defecation, the prolapse of the mucosa retracts and the sphincter exerts its full force. The gradually weakened condition of the sphincter is proportionate to the length of time the prolapse has existed, also relative to the size of the prolapse, and lastly, its persistence in remaining outside the anus. During the period of treatment in which the prolapsing mass is held within the rectum, the

sphincter tone is noted to improve continually, until by the tenth day the normal tone has been restored.

The general appearance of the prolapsed mass depends upon several factors. In the early stages of the simple mucosal type, the mucous membrane retains its normal color, and, as was earlier stated, appears in folds of mucosa about the anal margin. As the prolapse increases in age and size, it assumes a cone shape, base down, the rectal opening being at the peak of the cone. In neglected cases of rectal prolapse, the mucosa becomes thickened and edematous, and when it remains permanently outside the rectum, it is covered with alternating areas of glistening, dried mucous and blotched areas of hyperemia. The mucosa is denuded and replaced by areas of granulated tissue which have a tendency to bleed following bowel movements, contacts against clothing, and the movement of the thighs. Infections occur and heal over various areas of the prolapse at one and the same time. In extreme cases spotty areas of deep ulceration appear.

Complete or partial blocking of the return circulation in the prolapses is an accident that is only rarely seen. The retarded circulation is caused by the tight grasp of the sphincter muscle and this occurs only in those cases in which the sphincter tone is still active. In a delayed or late case of circulatory block the edema may increase the mass to the size of an orange. I have seen such a case in an adult in which the prolapse had reached the proportions of a child's head. The prolapse was of three days' duration and gangrene had developed to the extent that a resection was necessary as a life-saving measure. No such case as this had been seen in children, although a prolapse in which areas of blotchy discoloration had appeared had been reduced and returned within the anus without any bad effects. It is noted, in following this particular type of case, that the sphincter tone is very quick in recovering and that the tendency to recurrences is not as great as one would suppose.

Rectal polyps are often confused with prolapse and occasionally are the direct cause of a partial mucosal prolapse. In this latter type the base or pedicle of the polyp is low-lying, possibly just within the mucosal line, and the dragging down upon the polyp causes that area of the mucosa to which it is attached to be drawn down with it. The polyp and its adjacent mucosa may present and remain permanently prolapsed outside the anus. The differential diagnosis between a polyp and a mucosal prolapse is comparatively easy. Hemorrhage in the case of the polyp is far more profuse and usually recurs with each defecation. Instead of the generalized pinkish red of the mucosal prolapse, the color is characteristically described by the parent or attendant as resembling a piece of liver in color and consistency. On digital examination, the examining finger readily passes around the polyp and easily differentiates it from the surrounding mucosa. Pro-

lapsing rectal polyps are more frequently diagnosed as hemorrhoids than rectal prolapse, although no reasonable excuse exists for making this mistake.

In reviewing the authors' series of 32 cases, which were equally divided between the hospital and out-patient department, one is not impressed with any particular outside factor as an etiologic cause. It is true that prolapses occur frequently in the course of wasting disease in which the body fat is greatly reduced, but, on the other hand, hundreds of children have appeared for treatment in late stages of intestinal infections, in which diarrhea is the chief symptom, and loss of body fat is exceedingly great without the occurrence of prolapse. Pneumonia and prolonged bronchitis appear with about the same degree of regularity as a causative factor, as was noted by Lockhart-Mummery. The department of neurosurgery admitted for treatment 2 patients with a low spina bifida in which prolapse was present. The termination in both cases was fatal, but it is quite obvious that had the children lived no hopes could have been held out for a relief of the prolapse. In the genitourinary department, 2 patients with congenital stricture of the urethra, and 1 with an anomaly of the bladder with accompanying cystitis, finally developed rectal prolapse as a result of the severe and frequent straining at urination. Obviously the cure of the prolapsed rectum in these cases depends entirely upon the possibility of cure in the urinary organs. Unfortunately, the accompanying cystitis and general infection resulted in a fatal termination. One of these patients survived following successful treatment of a congenital stricture of the urethra. Irrespective of the stage of the disease or the time of appearance of the prolapse of the rectum, preventive treatment should be started at once.

TREATMENT

From the standpoint of treatment, children with rectal prolapse may be divided into two groups. The first is that large group appearing as ambulatory patients who otherwise seem to be perfectly well, and can be treated throughout as ambulant cases. The second group of children comprises those in which the prolapse develops during the period of pneumonia, bronchitis, or severe dysentery, necessitating the treatment of the patient in bed. In the group requiring bed treatment are the ambulant patients in whom the sphincter tone is so weakened that the prolapse cannot possibly be retained by any form of strapping. At any time it may be necessary to change a patient from the first or ambulant group, to the second which is continuously confined to bed. The mere placing of a child in a crib does not meet the requirements. The patient at all times throughout the period in bed, must be in a horizontal position. If this cannot be accomplished by ordinary persuasion, then the Bradford frame must be resorted to. It is essential

that the parent be fully informed as to the situation relative to the prolapse and to the details of treatment necessary to bring about recovery. It is important that the restoration of tone in the sphincter muscle be carefully explained so that the treatment may be logically carried out.

THE AMBULANT TREATMENT

Prolapse of the rectum is rarely neglected by the parent or attendant. The first occurrence usually results in a request for medical aid. Only rarely do we find neglected children in whom the prolapse has been present many weeks or months and has gradually been permitted to increase to unusually large proportions. If the sphincter tone is still fairly good and the prolapse tends to subside without the aid of manipulation, at the finish of the stool, then the patient can first be treated without confinement to bed. For a period of two weeks or possibly a month the child should be induced to evacuate the bowels either lying flat upon the back or on the side. The parent should be in constant attendance at all stools and should be instructed to compress the thighs and buttocks in order to prevent the prolapsing of the mucosa of the bowel. A flat bedpan may be utilized, but it may be necessary to pass the stool on a bed covered by a strip of rubber sheeting. Obviously, a considerable amount of soiling will take place, and the greatest care should be exercised in the cleansing of the skin. After a few successful days have passed the child may be permitted to use a modified seat cover, over a low stool.

The construction of such a toilet seat is very simple. In fact, the most serviceable examples of such seats have been made by the parents of the clinical patients. The materials selected have been thin pieces of board, carefully carved and showing excellent workmanship. Very satisfactory toilet seats have been made from celotex wall board and heavy pieces of cardboard. Rarely have the seats been improperly constructed after the parent has thoroughly understood exactly what was wanted. It is necessary to explain that a heart-shaped opening, similar in shape to the ordinary stool cover, be constructed, bearing in mind that the lateral measurements should be based upon the distance between the two ishia, and the anterior posterior measurements reduced in size to the same proportion. The exact measurements of such a seat made of cardboard measured 4½ inches across and 6½ inches in length. In full measurements, the seat cover should not extend more than 2½ inches beyond the margins of the vessel to be covered. This is important, since the child should be allowed to bring the legs well up against the margin of the vessel and thereby be able to assume a full squatting position. Attention is again called to the fact that a seat so constructed and placed over an ordinary stool prevents the spreading of the buttocks, but does not permit the flexing

of the thighs and the tensing of the perineum, which has been pointed out as of so much importance. The vessel should not be over 5 inches in depth thereby permitting a proper squatting posture. If at any time a recurrence of the prolapse should develop, a return to the lying position should be resumed and continued until all such signs have disappeared.

Strapping the buttocks together with adhesive is of considerable aid, and is carried out as follows: The child is placed upon the abdomen and a strip of adhesive 2 or 2½ inches wide is snugly fitted from trochanter to trochanter, with the buttocks pulled firmly together.

Fig. 1.—Homemade toilet seat constructed of piece of wall board by the parent of a child in the Out-Patient Department and used for two years. The child has fully recovered from prolapse of the rectum.

The skin should be well cleansed and dried before the adhesive is applied, and it is essential that there be no wrinkling of the adhesive. This leads to irregular pulling and skin irritation. The adhesive should be placed just low enough to avoid soiling at the stool, and the skin must be cleansed following each bowel movement, using the greatest care along the margin of the adhesive.

The plaster should be replaced at least every five days and in children with sensitive skins, or where the skin has become irritated by prolonged sickness, the change should take place daily. Considerable

time should be given at each change for a careful washing with soap and water to be followed by alcohol or ether, and a light powder. Great care should be taken that the alcohol or ether does not irritate or in any way cause the patient distress. The details given above are highly important since the adhesive strapping is such a great aid, particularly through the early days of the treatment for prolapse, and its abandonment greatly retards the improvement. Owing to nonpreventable skin irritation the adhesive cannot be used at all with some patients and attempts at holding the buttocks together must be made by fitting a tight binder completely about the body. After the patient has passed months without the recurrence of the prolapse there can be no reason for discontinuing the use of the seat cover, but the strapping of the buttocks should be discontinued in every case as soon as the prolapse remains within the rectum when the child is up and about, and is not brought on by sneezing, coughing, crying, or when at play. Obviously, the selection of a proper diet is absolutely essential. The morning stool must be soft and nonconstipating, and if necessary must be regulated by mild laxatives. Regularity is also important and the same hour should see the child at stool each day. If this does not come about naturally, it can soon be regulated with the aid of glycerine suppositories or low enemas.

Certain patients in whom the prolapse has been present over a long period of time, will not respond to this ambulant type of treatment. In these cases, it will be noted that the sphincter muscle is patulous and has not sufficient strength to hold back the prolapsing mucosa. Even with the buttocks strapped, upon the least exertion the prolapse will recur. It then becomes necessary to confine the patient to bed in the absolutely horizontal position. Usually the child is placed upon the back, but occasionally, in the hands of certain physicians, he is laid face downward. In my opinion the position in bed, aside from its horizontal nature, is not so important except in the case of the untrained or noncooperative child where resort to the Bradford frame may become necessary. The patient should be instructed to inform the attendant or parent if it is necessary to evacuate the bowel other than as usual in morning and evening. Even more important than in the ambulant type, it is necessary that the buttocks be pressed firmly together throughout the entire period of the evacuation, and whenever the prolapse recurs in spite of this care, it must be replaced immediately. All stools must be performed in the reclining posture, and it will be observed that by the tenth day the sphincter tone is sufficiently recovered so that the prolapse is supported. Whenever this time has arrived, the patient may be permitted to leave the bed but not to take part in strenuous play. Such a prolapse developing during an attack of pertussis may require the patient to remain in bed until the paroxysms of coughing have ceased.

The strapping of the buttocks is necessary even during the period that the child remains in bed and undoubtedly prevents many prolapses that would otherwise occur. Ten days in bed will so restore the tone of the sphincter muscle that the patient may be allowed up and treated as an ambulant case, although it may be necessary to continue the reclining position at stool for a much longer period of time, possibly two months. If recurrence takes place after this length of time, it then behooves the physician to be certain that he is not dealing with something more than an ordinary prolapse of the lower rectal mucosa. An intussusception, taking place at the rectosigmoid junction and presenting through the anus will not be improved by the treatment as outlined. Rectal polyps may be producing a mucosal prolapse and should be carefully ruled out. Malignant tumors in the lower pelvis are frequently accompanied by intensive straining and prolapse of the rectum. Occasional persistent recurrences can be cured only by abdominal operations, but these operations are often accompanied by a high operative mortality, and many disappointing relapses.

The replacement of the prolapsed rectum is very simple, as a rule. The retention following a replacement depends entirely upon the ability of the sphincter muscle to hold the prolapse in place. In cases of long standing, the thickening and edema of the prolapsed mass are such that by its own weight it drops down outside the anus. Occasionally, the physician is called in to treat a case of prolapse in which, on account of acute swelling, it is impossible to reduce the mass within the pelvis until it has first been reduced in size. In a small child from five to six years of age, the prolapse may reach the size of an orange, is discolored, and may show areas of gangrene. If the necrosis has advanced to the extent that recovery is not possible, then the only resort is surgical intervention, and complete amputation of the entire mass. This enormous size is reached or can be reached within twelve hours. I recall a patient in whom gangrene had developed in less than twenty-four hours, requiring resection. Every attempt should be made to reduce the size of the mass and reestablish the circulation. The arteries are continually pumping blood into the prolapse but the constriction offered by the sphincter muscle prevents the lymphatic and venous return, thereby accounting for the unusual size.

The entire prolapse should be bathed continually in warm cottonseed oil. A nurse should devote her entire time to the application of hot packs, firm pressure, and massage. The child should be placed in bed, face down, and the body jack-knifed over several pillows. The heated oil should be applied often enough not to allow any areas of the mucosa to become dry—at least every ten or fifteen minutes. Soft compresses wrung from hot saline and applied to the area with the firm pressure of the nurse's hand are of the greatest aid. Com-

presses simply wrung out and applied or covered with a hot water bottle are of little help, and only by the compact pressure of the applications is the edema forced out of the tissues. Gentle massage with firm compression from the tip of the prolapse to the base, hastens the reduction, and in from four to six hours it may be possible to reduce the mass within the sphincter. After the sphincter is once passed, the edema is readily carried off as all the constrictions are removed, and the physician's only worry is a recurrence of the prolapse.

When the prolapse is the size of a lemon but offers such resistance that the parent is unable to make a reduction, the physician, in the course of half an hour, may be able to bring it about. The child is held across his lap resting on a pillow, the head slightly down and the legs spread on either side of the physician's body. In this posture, gravity favors the return circulation as well as the replacement of the mass. With the gloved hand well lubricated, a gentle compression massage is started, aided by hot compacts, and within a comparatively few minutes the mass is reduced. Resistance may be kept up by an unruly child for some time, but with the legs held firmly, the patient soon realizes that resistance is useless and so remains quiet. Firm pressure is essential, but impatience is to be guarded against and at no time should the reduction of the edematous mass be painful. Rather, the gentle massage, the soothing effect of the oil, and the heat, should tend to give relief from pain and afford comfort to the patient. As soon as the reduction is completed, the buttocks should be strapped with adhesive and the child confined to the bed. It is to be remembered that although the sphincter tone may have quickly recovered, the edema in the bowel wall will have a tendency to increase the possibility of further prolapse until the edema has entirely disappeared.

CONCLUSIONS

1. Prolapse of the rectum in children, otherwise normal, tends to spontaneous recovery.

2. The suggestions of Lockhart-Mummery for the nonoperative treatment of prolapse of the rectum in children are successful and practical when the treatment is properly carried out.

3. The literature so emphasizes the many operative procedures for prolapse that the nonoperative treatment is never dealt with at sufficient length to set forth its value.

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DENVER'S INFANT MORTALITY

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DENVER, COLORADO

IN 1915 the infant mortality rate for the United States Registration Area was 99.9 per 1,000 live births; and the rate for Denver was 91.3 per 1,000 live births.

By 1928 the infant mortality rate in the United States Registration Area had fallen below 70, but that of Denver was still 91 per 1,000 live births, thus placing it in the unenviable position of being at the bottom of a group of 25 cities with a population of 250,000 or over, while Portland, Oregon, and Seattle, Washington, stood at the top with an infant mortality rate of only 43 per 1,000 live births; less than half the rate of Denver.

TABLE I

INFANT MORTALITY RATES

Denver	1915	91	1928	91
United States Registration	1915	100	1928	69
New York	1917	89	1928	59
Cleveland	1917	109	1928	60
Minneapolis	1917	71	1928	51
Omaha	1917	75	1928	56
Portland	1917	62	1928	43

In an effort to discover the cause for this persistently high rate in Denver there was organized a survey of all births occurring in Denver for a year extending from March 1, 1930, to February 28, 1931 (inclusive); and arrangements were made for an analysis of the deaths occurring in the infants in this group within a year of their birth.

As a preliminary to this survey a questionnaire of 150 items was formulated by a committee of physicians, health officers, nurses, and social workers, which was given a month's trial in the births occurring during the month of February, 1930.

The field work was done by the Visiting Nurses Association of Denver, in cooperation with the physicians delivering the infants and the hospitals in which the larger number of the infants were born.

The statistical work was done by Dr. A. D. H. Kaplan, head of the University of Denver Bureau of Research, and Professor F. L. Carmichael, head of the University of Denver Bureau of Statistics.

In a previous paper ("Infant and Maternal Mortality in Denver," JOURNAL OF PEDIATRICS, December, 1932) a preliminary report for the

President's address, Section on Pediatrics, Pan-American Medical Congress, March 21-25, 1933, Dallas, Texas.

first six months of this survey was given, and it now seems timely to give some of the results for the entire year.

During the period covered by this survey there occurred 5,330 live births; 180 stillbirths; 410 infant deaths; and 41 maternal deaths—or a stillbirth rate of 33.77 per 1,000 live births; an infant mortality rate of 77 per 1,000 live births; and a maternal mortality rate of 7.7 per 1,000 live births.

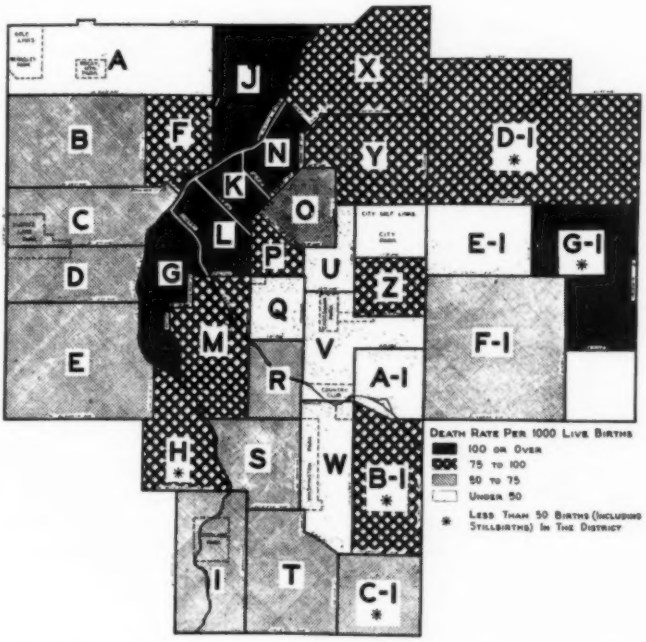

Fig. 1.—Infant death rate by districts. (Courtesy Bureau of Business and Social Research, University of Denver, and *The Trained Nurse and Hospital Review.*)

The corresponding rates in the United States Registration Area for 1930 were stillbirths 39, infant mortality 65.6, and maternal mortality 5.8 per 1,000 live births.

Of the 5,330 live births, 895, or 17 per cent of the total, were the offspring of parents who were nonresidents of Denver. While it proved impossible to follow all of these infants in the nonresident group for the whole year following their birth, the study showed that 55 were reported as having died within a year of their births, or a mortality rate of 61 per 1,000 live births.

In the remaining 4,453 live births, residents of Denver, there were 345 infant deaths, or a mortality rate of 77 per 1,000 live births.

MORTALITY BY DISTRICTS

The accompanying graph (Fig. 1) and Table II show the marked variation in the infant mortality rate in the 33 districts into which the city is divided for social service purposes, ranging as it did from 24 per 1,000 live births in District A, to 210 in District K.

In the 5 best districts (A, E-1, Q, W, and A-1) the composite rate was 32 per 1,000 as compared with a rate of 190 per 1,000 in 5 of the worst districts (K, G, L, N, and J)* which form a black belt along the bottoms of the Platte River. It is in this area that family incomes are lowest, housing accommodations are poorest, and sanitation most lacking.

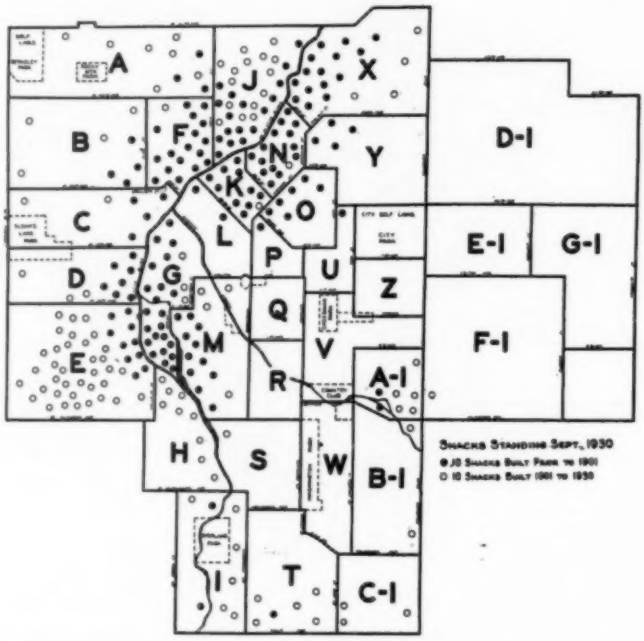

Fig. 2.—Location of shack-housing as of September, 1930. (Courtesy Bureau of Business and Social Research, University of Denver, and *The Trained Nurse and Hospital Review.*)

POOR HOUSING

Fig. 2 best illustrates the lack of proper housing accommodations, showing the number of shacks appraised at less than $200 in each district; each solid black dot representing 10 such shacks built prior to 1901, and each circle 10 such shacks built between 1901 and 1930.

District G showed the greatest concentration of old shacks, 224 in number; and a survey revealed that 86 per cent of all the homes in District G, 91 per cent of the homes in District N, and 89 per cent of the homes in District K were built prior to 1901.

*District G-1 which had a rate of 128 as compared with 106 for District J, is not included, as it is very sparsely settled and had less than 50 births including stillbirths.

TABLE II

DEATH RATES BY DISTRICTS

DISTRICT	NUMBER OF L. B.	NUMBER OF DEATHS	RATE PER 1,000 L. B.	DISTRICT	NUMBER OF L. B.	NUMBER OF DEATHS	RATE PER 1,000 L. B.
A	167	4	24	V	134	6	45
B	291	18	62	W	104	4	38
C	109	8	73	X	86	7	81
D	154	9	58	Y	209	16	77
E	188	11	59	Z	119	11	92
F	238	18	76	A-1	50	2	40
G	172	35	203	B-1	36	3	83
H	35	3	86	C-1	33	2	61
I	51	3	59	D-1	24	2	83
J	123	13	106	E-1	103	3	29
K	100	21	210	F-1	49	3	61
L	72	13	181	G-1	39	5	128
M	403	31	77				
N	149	27	181	Total	4,371	350	81
O	208	15	72				
P	150	13	87	Denver Unclassified	25	3	120
Q	142	5	35	Out-of-Town Cases	895	55	61
R	130	9	69	Not Reported	39	2	51
S	172	12	70				
T	219	13	59	Total	959	60	63
U	112	5	45				
				Grand Total	5,330	410	77

TABLE III

INCOME	NUMBER OF DEATHS	RATE PER 1,000 L. B.	INCOME	NUMBER OF DEATHS	RATE PER 1,000 L. B.
Under $500			*$2,000 and under $2,500*		
Under 2 wk.	14	51	Under 2 wk.	11	27
2 wk. to 1 yr.	34	125	2 wk. to 1 yr.	7	17
Total	48	176	Total	18	44
$500 and under $1,000			*$2,500 and under $3,000*		
Under 2 wk.	31	37	Under 2 wk.	8	33
2 wk. to 1 yr.	49	59	2 wk. to 1 yr.	4	16
Total	80	96	Total	12	49
$1,000 and under $1,500			*$3,000 and above*		
Under 2 wk.	47	43	Under 2 wk.	8	22
2 wk. to 1 yr.	31	28	2 wk. to 1 yr.	1	3
Total	78	71	Total	9	25
$1,500 and under $2,000			*All income groups (including NOT REPORTED)*		
Under 2 wk.	22	28	Under 2 wk.	216	41
2 wk. to 1 yr.	23	29	2 wk. to 1 yr.	188	35
Total	45	57	Total	404	76

FAMILY INCOME FACTOR

That the amount, or rather the lack of amount of family income is a very large factor in influencing the infant mortality rate is well shown in Table III.

There was a rate of 176 per 1,000 live births in the income group with less than $500 a year, as compared with a rate of 25 in the group with an income of $3,000 or above. This table shows that most of the deaths in the lower income group occur after the first two weeks while those in the higher income group occur in the first two weeks. The high income group shows a very low infant mortality rate later in the year. A natural inference would be that this large variation is due to the lack of sufficient income to provide the infant with proper food, and the necessary medical and nursing care so essential to its proper development and continued welfare during its first year; the dividing line apparently being between $1,500 and $2,000 a year or about $150 a month.

Table IV shows the infant mortality and average para by income groups with the higher average paras occurring as is usually the case in the lower income groups.

TABLE IV

INFANT MORTALITY AND AVERAGE PARA BY INCOME GROUPS

ANNUAL FAMILY INCOME	NUMBER OF LIVE BIRTHS	NUMBER OF DEATHS	RATE PER 1,000 L. B.	AVERAGE PARA
Under $250*	56	4	72	4.12
$ 250 to $ 500	218	44	202	3.71
$ 500 to $ 750	398	40	101	3.18
$ 750 to $1,000	440	58	91	2.96
$1,000 to $1,250	767	20	76	2.70
$1,250 to $1,500	337	45	59	2.60
$1,500 to $2,000	790	18	57	2.42
$2,000 to $2,500	408	18	44	2.22
$2,500 to $3,000	247	12	49	2.36
$3,000 to more	363	9	25	2.39
Not reported	1,306	120	92	2.04†
All Incomes	5,330	410	77	2.54

*Charity cases included.

†Based upon 1,173 cases only, since para information was lacking on 133 cases in this group.

Table V shows the infant mortality classified by para. As might be expected the higher rates occur in the higher paras, and range from 64 in para i to 220 in para ix.

MORTALITY IN FIRST DAY

In 1930 the infant mortality rate for the United States Registration Area was 64.6 per 1,000 live births compared with Denver's rate of 77 during the survey year; and during the first twenty-four hours the corresponding rates were 15.0 compared with 25.7 for Denver. Strangely enough the survey showed that while there was a total of

TABLE V

INFANT MORTALITY IN DENVER CLASSIFIED BY PARA

(Denver Residents Only)

PARA	LIVE BIRTHS	DEATHS	RATE PER 1,000 L. B.
1	1,623	104	64
2	1,047	69	66
3	640	46	72
4	363	26	72
5	249	28	112
6	148	24	162
7	101	14	139
8	54	8	148
9	50	11	220
10 or more	71	11	155
Not reported	25	9	360
Total or Average	4,371	350	80

109 infant deaths during the year in the five "black belt" districts, only 21 deaths (19 per cent) occurred in the first twenty-four hours, while in the 5 best districts, 12 of the total of 23 deaths occurred in the first twenty-four hours, or 52 per cent. This would indicate that the influence of high or low family income begins to show itself sometime later in the first year.

TABLE VI

NEONATAL MORTALITY

(Total Live Births—5,330)

	NUMBER OF DEATHS	RATE PER 1,000 L. B.	U. S. REGISTRATION AREA	
			1929	1930
First Day	137	25.7	15.3	15.0
First Week	201	37.7	28.0	27.2
First Two Weeks	216	40.5	31.9	31.1
First Month	240	45.0	36.9	35.7
First Three Months	311	58.3	46.8	45.2
First Six Months	362	67.9	56.0	53.9
First Year	410	76.9	67.6	64.6

In Table VI is shown the high percentage of infant deaths in the first month of life; 240 out of a total of 410 infant deaths, or 45 per 1,000 live births (more than one-half for the whole year); and a comparison with the rates for the United States Registration Area in 1929 and 1930.

TABLE VII

NEONATAL CAUSES OF DEATH

	DENVER	U. S. REG. AREA (1929)
Premature	24.4	16.8
Birth Injury	4.9	4.7
Congenital Malformations	3.4	4.1
Pneumonia	2.4	1.5
All Other Causes	9.9	9.8
Total	45.0	36.9

In Table VII is shown the principal causes of neonatal deaths (under one month) with the corresponding rates for the United States Registration Area (1929), per 1,000 live births.

This table shows that the rates for prematurity and pneumonia in Denver were both about 50 per cent higher than in the United States Registration Area.

INFLUENCE OF PRENATAL CARE

One of the most striking findings in the survey was the apparent influence of prenatal care of the mother upon the infant mortality rate.

TABLE VIII

INFANT MORTALITY IN DENVER

(Classified by Prenatal Visits)

NUMBER OF PRENATAL VISITS	LIVE BIRTHS	DEATHS*	RATE PER 1,000 L. B.
None	375	74	198
1 or 2	846	109	129
3 or 4	692	73	105
5 or 6	678	49	72
7 or 8	758	33	44
9 or more	1,162	35	30

*Stillbirths not included.

The family income factor is probably also shown in Table VIII, since the group of live births whose mothers had had no prenatal visits showed an infant mortality rate of 198 per 1,000 live births, as compared with a rate of 30 in the group in which the mothers had had 9 or more prenatal visits.

Table IX shows the percentage distribution of prenatal visits among the stillbirths, the live birth deaths, and the live births exclusive of deaths. This table would indicate that most of the infants who lived through their first year were born to mothers who had had the benefit of 5 or more prenatal visits.

TABLE IX

PERCENTAGE DISTRIBUTION OF PRENATAL VISITS

NO. OF VISITS	LIVE BIRTHS EXCLUSIVE OF DEATHS		LIVE BIRTH DEATHS		STILLBIRTHS	
	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
None	299	6.1	74	18.0	24	13.5
1 or 2	737	15.0	109	26.6	36	20.2
3 or 4	619	12.6	73	17.8	32	18.0
5 or 6	629	12.8	49	12.0	20	11.2
7 or 8	725	14.7	32	7.8	28	15.7
9 or more	1,127	22.9	35	8.5	24	13.5
Not reported	784	15.9	38	9.3	14	7.9
Total	4,920	100.0	410	100.0	178	100.0

RACIAL FACTOR

The survey showed very definitely that the infant mortality rate was unquestionably increased by the very high mortality rate in the Mexican race.

TABLE X

COMPARISON OF DEATH RATES BY RACES

	TOTAL	WHITE	BLACK	MEXICAN	YELLOW	NOT REP.
Live Births	5330	4804	96	294	14	122
Infant Deaths	410	335	6	57	2	10
Infant Death Rate	77	70	63	194	143	82
Stillbirths	189	152	5	18	0	4
Stillbirth Death Rate	35	32	52	61	0	33
Maternal Deaths*	39	36	0	3	0	0
Maternal Death Rate	7.3	7.5	0	10.2	0	0

*Includes deaths in which maternity was only a contributory cause.

"The Mexican population formed less than 3 per cent of Denver's total, but its infant mortality comprised 14 per cent of all the infant deaths in the city. Out of 294 Mexican live births (or 5.5 per cent of the total births) 185 or 63 per cent occurred in the Platte River bottoms, where the Mexicans registered an infant mortality rate of 232 per thousand, against 81.9 per thousand for the non-Mexican births in the same districts."*

Table XI shows the racial distribution of full-term and premature stillbirths.

TABLE XI

	FULL TERM	PREMATURE	TOTAL
White	76*	76	152
Mexican	9	9	18
Black	4	1	5
Not reported	1	3	4
Total	90	89	179

*Included 2 cesarean sections.

TABLE XII

AGE OF MOTHER

	LIVE BIRTHS	DEATHS	RATE
Under 20	720	75	104
21 and under 25	1,727	127	74
25 and under 30	1,385	89	64
30 to 35	874	57	65
35 to 40	466	37	79
40 to 45	124	17	137
45 and over	5	0	0
Not reported	29	8	276

*Infant Mortality as an Index of Community Welfare by A. D. Kaplan, Ph.D., Denver, Colorado, Am. J. Public Health, October, 1932.

MOTHER'S AGE

Table XII shows the infant mortality in relation to the mother's age at the time of delivery, the higher rates being in mothers under twenty years of age and those over forty years of age.

INFANT'S DEATH RATES BY CAUSES

Fig. 3 shows that the most common cause given for the infant deaths was prematurity, 32.2 per cent of the deaths, or a death rate of 24.6 per 1,000 live births in Denver as compared with 17.4 (1927-1928 average) for the United States Registration Area.

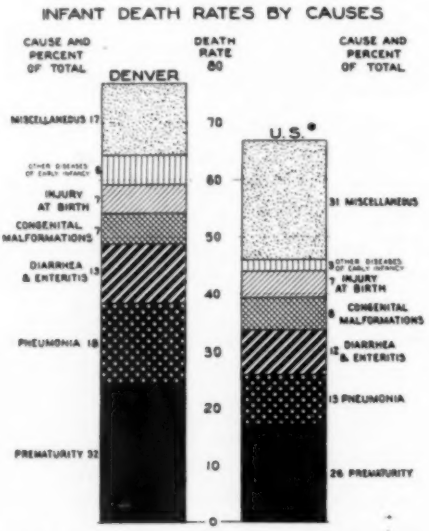

Fig. 3.—Infant death rates by causes. (Courtesy Bureau of Business and Social Research, University of Denver, and *The Trained Nurse and Hospital Review.*)

*Average 1927-28.

The second largest cause given was pneumonia, 18 per cent as against 13 per cent for the whole country, or a rate of 14 per 1,000 live births as compared with 8.9 (1927-1928 average).

One of the unexpected findings in the study was the infrequency of tuberculosis as a cause of infant mortality in Denver with 1 case in the 410 deaths or 2.44 of every 1,000, whereas the United States Census for 1928 showed 1,227 infant deaths due to tuberculosis in the United States Registration Area, or 8 of every 1,000 infant deaths.

The causes of infant deaths by percentages for the United States

Registration Area in 1930 (survey year) are practically the same as those for 1927-1928 in the graph, and are as follows:

	DENVER (SURVEY YEAR)	UNITED STATES REGISTRATION AREA 1927-1928	1930
Prematurity	32	26	25.8
Pneumonia	18	13	13.7
Diarrhea and Enteritis	13	12	12.1
Congenital Malformation	7	8	8.2
Injury at Birth	7	7	7.5
Other Diseases in Early Infancy	6	3	3.4
Miscellaneous Causes	17	31	29.3
Total	100	100	100.0

Table XIII shows a comparison of the fetal and neonatal (under 2 weeks) deaths in mothers, 27 per cent of whom were confined at home and 73 per cent in the hospital. The difference in the rates is not remarkable.

TABLE XIII

	NUMBER		RATE PER 1,000 L. B.	
	HOME	HOSPITAL	HOME	HOSPITAL
Fetal Deaths	45	131	31	34
Under 2 weeks	64	152	44	39

TABLE XIV

USE OF ANALGESIA AND ANESTHESIA

(Total Cases Only)

	LIVE BIRTHS	NEONATAL DEATHS	RATE
No Aid	1,290	91	70.5
Analgesia Only	53	8	150.9
Anesthesia Only	2,575	94	36.5
Both Analgesia and Anesthesia	185	13	70.3
Total Sedations	2,813	115	40.9
Not reported	1,227	34	27.7
Total	5,330	240	45.0

TABLE XV

BIRTH AND LABOR

(Total Cases Only)

	LIVE BIRTHS	NEONATAL DEATHS	RATE	FIRST YEAR DEATHS	RATE
Spontaneous	3,341	156	47	276	83
Pituitary Extract	511	12	24	25	49
Ergot	182	4	22	13	71
Castor Oil and Quinine	142	5	35	7	49
Other and Unknown	548	19	35	26	47
Forceps—High	36	2	56	2	56
Mid	50	2	40	2	40
Low	323	14	43	17	53
Version and Extraction	21	5	238	5	238
Breech Extraction	67	13	194	14	209
Cesarean Section	64	9	141	12	188
Nonspecific Aid	54	2	37	3	56
Not reported	996	28	28	60	60

Table XIV shows the neonatal deaths in relation to the type of sedative, if any, used during labor, and indicates the value of anesthesia during labor.

Table XV shows the influence on the infant mortality of instrumentation and the use of other measures to promote the birth of the infant. The higher rates were naturally found in the cases with version and extraction, breech extraction, and cesarean section. Contrary to popular belief the rates in cases where forceps were used proved quite low.

Table XVI shows the influence of a few of the most serious accidents occurring during labor on the neonatal and infant mortality.

TABLE XVI

LABOR ACCIDENTS

(Total Cases Only)

	LIVE BIRTHS	NEONATAL DEATHS	RATE	FIRST YEAR DEATHS	RATE
Normal	3,043	143	47	227	75
Placenta Previa	16	3	188	4	250
Prolapsed Cord	9	1	111	1	111
Hemorrhage	166	13	78	18	108
Other Accidents	25	6	240	6	240
Not reported	2,080	75	36	156	75

Table XVII shows the mortality statistics dependent upon the condition of the infant at birth.

TABLE XVII

CONDITION AT BIRTH

	LIVE BIRTHS	NEONATAL DEATHS	RATE	FIRST YEAR DEATHS	RATE
Color:					
Good	3,992	65	16	197	49
Poor	424	141	333	153	361
Not reported	914	34	37	60	66
Respiratory Cry:					
Spontaneous	3,657	104	28	220	60
Induced	509	87	171	101	198
Not reported	1,164	49	42	89	76

EFFORTS TO REDUCE INFANT MORTALITY

Impressed with the startling infant death rate in Denver's "black belt," "Shack Town" area along the Platte River "bottoms," the Mayor and Manager of Public Health have wiped out many of the least inhabitable old shacks, and with the cooperation of the Denver Real Estate Exchange many of "Shack Town's" inhabitants have been moved to housing of a better grade with lowest possible rents.

Denver as a whole has apparently become more "health minded," and, through the increased efforts of the physicians of Denver, ably aided by the Visiting Nurses Association and other social service or-

ganizations, seems at last to be showing some definite results in reducing its inordinately high infant mortality rate, as is shown in Table XVIII.

TABLE XVIII

BIRTHS AND DEATHS IN DENVER, COLORADO*

(Rate per 1,000 Live Births)

	1930	1931	1932
Live Births	5,273	4,702	4,866
Infant Deaths	496	356	377
Rate	94	76	69
Stillbirths	175	143	139
Rate	33	30	29

*Denver Health Department Statistics. All infant deaths in Denver during the year, including nonresidents.

We believe these better statistics are a result of the educational interest aroused by the survey and should be an inspiration to other cities of too high infant mortality "to go and do likewise."

IDIOPATHIC DILATATION OF THE COMMON BILE DUCT IN CHILDREN

Review of the Literature and Report of Two Cases

Robert E. Gross, M.D.
Boston, Mass.

CASE REPORTS

Case 1.—A four-year-old white girl with attacks of abdominal pain, vomiting, jaundice, and acholic stools for three months. Liver enlarged. Large tumor palpable in the right upper quadrant of the abdomen. At operation the common duct was found to be spherically dilated to 13 cm. in diameter. Dilated common duct anastomosed to the duodenum. Patient symptom-free four years after operation.

History.—M. H., a white girl, aged four years and five months, entered the hospital on August 21, 1928. For three months before admission there had been attacks of vomiting associated with midepigastric pain which was noncolicky in nature and which would last from a few minutes to an hour or more. Such attacks had no fixed relationship to meals, occurring both before and after eating. The frequency of attacks was irregular, appearing as often as several times a day, while at other times she would be symptom-free for two or three weeks. Shortly after the onset of these symptoms she became jaundiced. Though the jaundice had been constantly present during the three months, it seemed to vary in intensity. The stools had been clay colored for the entire three months and the urine had been darkly colored. There had been weakness and loss of vitality during the few weeks previous to hospital entry.

Physical Examination.—A marked jaundice was present. The abdomen was full but not distended. The liver edge was felt 5 cm. below the right costal border. A large epigastric mass was palpated which was at first thought to be the left lobe of the liver. Temperature 98.6° F. Pulse 90. Respirations 20.

Laboratory Studies.—Blood hemoglobin 80 per cent (T). Red blood count 4,700,000. White blood count 13,300. Tuberculin test negative in dilution of 1:1000. Urine contained large amounts of bile. Stool was clay colored and was free from bile pigment.

X-rays of the abdomen were negative for cholelithiasis and barium studies of the gastrointestinal tract gave no evidence of a pathologic condition.

Course.—The jaundice spontaneously receded in intensity and in two weeks the stools were normally brown colored. In three weeks the urine gave negative tests for bile pigments. Because of the general improvement, the patient was discharged on September 16, 1928 with a diagnosis of (?) catarrhal jaundice.

She was seen at frequent intervals until March 4, 1929 when she again entered the hospital. Since discharge, jaundice had recurred and had been present for five months, though it had varied in intensity. The stools had been intermittently clay colored. For the last month before reentry there had been a gradually increasing prominence of the abdomen, particularly in the right upper quadrant. This mass was smooth, rounded, firm, nontender, and descended during inspiration. Twice, within the month before reentry, the patient had experienced abdominal pain similar

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to that which she had had before the first hospitalization. The pain was located about the umbilicus, lasted about ten minutes each time of appearance, and was relieved by spontaneous vomiting. The veins over the abdominal wall had become enlarged and engorged. With the diagnosis of congenital cyst of the common bile duct, operation was advised.

Operation.—March 13, 1929. A spherical mass about 13 cm. in diameter lay behind the gallbladder and toward the midline. The duodenum and the mass, which was obviously a cyst of the common duct, were approximated to each other, were opened, and an anastomosis made. A cigarette drain was put down behind the anastomosis. A catheter was left in the gallbladder, and the abdominal wall was closed about the drains and catheter.

Convalescence.—The jaundice cleared up rapidly and on March 28, 1929, the icteric index was 7. The stools became normal in appearance in several days, and the urine was free from bile pigments on March 17 and thereafter. She was dis-

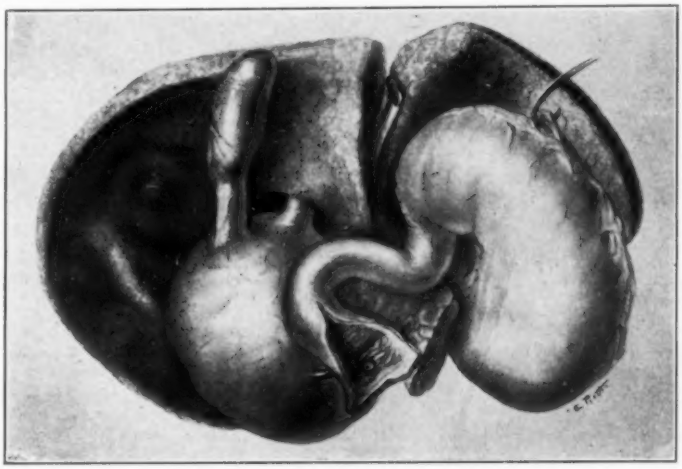

Fig. 1.—Cystic dilatation of the common bile duct (Case 2). Enlarged cystic and hepatic ducts may be seen entering the upper portion of the "cyst," while the lower portion of the common duct is of normal caliber and normally enters the ampulla of Vater. The dilated portion of the common duct measured 7 cm. in diameter and 12 cm. long.

charged on April 18, 1929, and was symptom-free. The patient was last seen in July, 1933, and at that time was perfectly well and without complaint.

Case 2.—A three-year-old white girl with abdominal swelling for one year and jaundice for three weeks. At a first operation the mass was erroneously thought to be a neoplasm and a biopsy specimen was taken from the liver. At the second operation (six weeks later) a cystic dilatation of the common duct was found. This structure was approximately 7 cm. in diameter and 12 cm. long (Fig. 1). Attempt to excise the "cyst" and to establish external drainage of the hepatic duct resulted in death.

History.—M. T. H., a three-year-old white girl, entered the hospital on July 6, 1931. During the year previous to entry a progressive enlargement of the abdomen had been noted, but because of otherwise good health the swelling had been disregarded. For three weeks before entry the patient had had jaundice, weakness, and anorexia. At the onset of jaundice the stools became clay colored. Further

questioning revealed the fact that one year previously there had been an attack of jaundice and anorexia, lasting two or three days, but because of the brevity and mildness of symptoms, medical advice had not been sought. At no time had there been pain, vomiting, or fever.

Physical Examination.—A slight jaundice was present. The thorax was symmetrical but was flared out below the level of the nipples, giving the impression that a large intraabdominal mass was pushing up the diaphragm and bulging out the lower part of the thoracic cage. Prominent veins coursed over the anterior abdominal wall. The liver edge could be palpated 5 cm. below the right costal margin. The liver edge and surface felt finely nodular, and palpation of the liver was nontender. The tip of the spleen could be felt 5 cm. below the left costal border. In the umbilical region, an indefinite mass could be palpated, which locally distended the abdominal wall. This mass was rounded, about 6 cm. in diameter, nonmovable, and nontender.

Laboratory Data.—Red blood count 5,600,000. White blood count 12,100. Hemoglobin 50 per cent (T). Examination of the urine gave a positive bile test. The tuberculin test was negative in a dilution of 1:500. Icteric index 30. Intravenous skiodan cast normal appearing shadows of the renal pelves and ureters.

Course.—Reexamination of the abdominal mass at frequent intervals gave the impression that it varied in size, but little attention was paid to this fact at the time. During the course of a week the jaundice spontaneously disappeared. Abdominal exploration was advised with the diagnosis of (?) abdominal neoplasm.

First Operation.—July 15, 1931. A large retroperitoneal mass was discovered which was thought to be a neoplasm. No attempts were made at removal, for the liver was studded with small nodules which were erroneously thought to represent metastases. A small piece of liver was removed for pathologic examination and the abdominal wall was closed.

Microscopic examination of the liver specimen showed the terminal stages of repair of a hepatitis (Fig. 3). Because the microscopic section failed to show any neoplasm within the liver, a second operation was undertaken for removal of the retroperitoneal mass.

Second Operation.—August 28, 1931. A large, tense, smooth, rounded mass was found lying to the right of the mesenteric root, extending up into the right upper quadrant in the region of the bile ducts. This mass was now found to be definitely cystic, and measured about 7 cm. in diameter and 12 cm. long (Fig. 1). Believing it to be a retroperitoneal cyst, enucleation was begun. Needle puncture of the sac produced bile, and incision of the structure revealed two openings at the upper pole which were the slightly enlarged cystic and hepatic ducts. The outlet of this greatly enlarged common duct was not found at operation. Enucleation had proceeded too far and the child's condition did not permit an anastomosis with the duodenum. The only procedure then possible was to remove the "cyst" completely and to place catheters in the cystic and hepatic ducts for external drainage, with the idea of anastomosing the hepatic duct with the duodenum at a later operation. The child's postoperative condition was very poor and she died seven hours later.

Pathologic Reports of Case 2.—The cyst wall (which was removed at operation) was dense, fibrous, and varied from 1 to 3 mm. in thickness. The internal surface was roughened, yellowish gray, and supported many small soft, reddish brown elevations 3 to 4 mm. in diameter and 1 to 2 mm. in height, which appeared to be areas of necrosis and hemorrhage. Microscopic examination of the cyst wall showed it to be composed of dense fibrous tissue without epithelial lining and with only a thickening of connective tissue to form the inner layer (Fig. 2). There was no

smooth muscle present. Through the wall coursed numerous small blood vessels, some of which were thrombosed and recanalized. There were occasional hemorrhages, and scattered throughout the sections were polymorphonuclear leucocytes and lymphocytes which in places were massed in large numbers.

The necropsy findings of interest were limited to the upper abdomen. The cystic, hepatic, and lower portion of the common duct had all been cut across when the "cyst" was removed at operation. The lower, remaining portion of the common duct was picked up by passing a probe through the ampulla of Vater, and by this examination was found to be unobstructed, with normal-sized lumen, and measured about 4 cm. in length. Its proximal end was severed and was lying free in the gastrohepatic ligament. The hepatic duct was dilated to 1 cm. in diameter up to the place where it entered the liver, but had a normal caliber above this level. The cystic duct was enlarged, but the gallbladder was only 5 cm. long and 1½ cm. in greatest diameter.

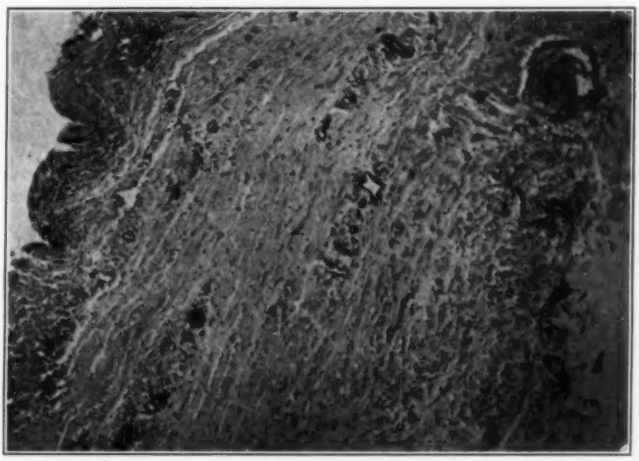

Fig. 2.—Photomicrograph of the common duct "cyst" wall; ×100. The inner surface of the "cyst" is at the left side of the photograph. The wall is composed of connective tissue. There is no epithelial lining, only dense fibrous tissue forming this inner layer. Smooth muscle is absent. Some areas show mild leucocytic infiltration.

The liver was very hard and the entire surface was studded with small nodules from 2 to 3 mm. in diameter. The entire liver substance was grayish green, but the nodules were of a slightly darker hue than the tissue surrounding them. On section of the organ, there was an extensive cirrhosis with regeneration of the liver parenchyma. No central veins could be seen. There was no dilatation of the intrahepatic ductal system.

In the microscopic sections it was interesting to note the progress of liver repair which had taken place in the six weeks since the biopsy of the liver at the first operation. The specimen removed at the first operation showed a healing hepatitis, with sharply circumscribed islands of regenerated parenchyma surrounded by wide zones of dense periportal connective tissue in which there were numerous proliferating bile ducts (Fig. 3). In the autopsy liver specimen the cells were more mature and the hepatic cords were now distinct and well formed while the lobular structure more closely approximated the normal (Fig. 4). During this period of six weeks the periportal connective tissue had decreased in amount and density.

The gallbladder showed evidence of mild acute cholecystitis with some minor changes indicative of chronic infection. The mucosal vessels were congested, and throughout the mucosa there were a small number of polymorphonuclear leucocytes. The entire gallbladder was mildly edematous. The serosa, and subserosal layer contained scattered polymorphonuclear leucocytes, eosinophiles, and lymphocytes.

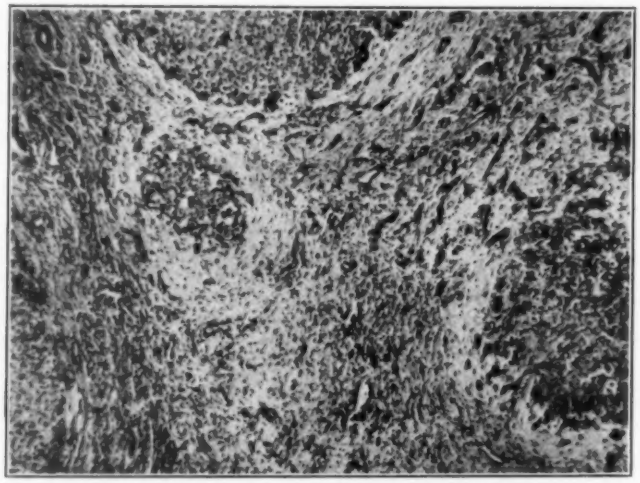

Fig. 3.—Photomicrograph of liver specimen removed at the first operation: ×100. An extensive cirrhosis is present. The liver cells are regenerating but are still immature. The liver cords are not yet formed. There are wide zones of periportal connective tissue in which there are numerous proliferating bile ducts.

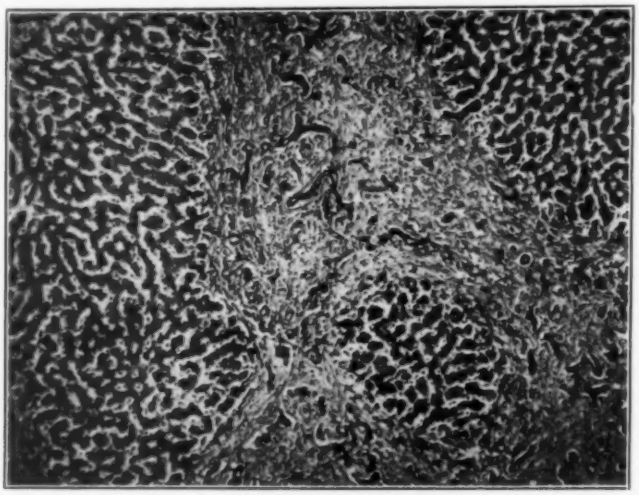

Fig. 4.—Photomicrograph of liver as found at autopsy; ×100. Autopsy section taken six weeks after the specimen which was removed at operation (Fig. 3). The liver cells are now more mature and the liver cords are well formed. Cirrhosis is still present, but the amount of connective tissue is less than noted formerly. Proliferating bile capillaries are still prominent.

The pancreas was of normal consistency and grossly there was no evidence of pancreatitis. Microscopically, there was an essentially normal structure. There was no abnormality of the ductal system.

The spleen was moderately enlarged and fibrosed, these findings being interpreted as secondary to the obstruction of portal circulation by the liver cirrhosis.

REVIEW OF LITERATURE

Zinninger and Cash in January, 1932, reviewed 83 cases of choledochus cyst occurring in all age groups. They excluded the case of Fowler as not being a true case of idiopathic cyst, but we (with Judd and Greene and others) believe it should be included in a review. Zinninger and Cash mentioned the cases of di Natale, Jauregui, Olivecrona, Stoney, Sieber, and Zaczek, but did not include them in their series because original articles or satisfactory reviews were not available. We have reviewed the first 5 of these cases and include the first 4 as being true cases of idiopathic dilatation of the common bile duct. There are 10 other cases not mentioned by Zinninger and Cash (some of these have been published since their article was completed); Badile, Choyce, Erdély (2 cases), Ladd (2 cases) (from this clinic), Morley (a second case), Morrin, Terada and Vagi, and Young. Thus, with the 2 cases herein reported, there is a total of at least 100 cases at all ages now in the literature.

Of these 100 cases in the literature, 52 occurred in childhood or had symptoms which had persisted since childhood. The cases of Dreesman, Ebner, Fenger, McWhorter, and Taylor are included, for while these patients were twenty-four, eighteen, seventeen, forty-nine, and twenty-three years old respectively, they all had had symptoms since childhood. Sixty-six original papers concerning choledochus cysts have been read, and of the 50 cases previously reported in childhood, we have referred to original papers in 37 instances and reviews in 3 cases. Original articles or reviews of the remaining papers are not accessible to us, and citations are made from Waller, McWhorter, Zinninger and Cash, and Seneque and Tailhefer; 4, 2, 1, and 3 cases being cited respectively from these authors.

PATHOLOGY

Dilatation of the common duct is the characteristic finding and takes the form of a spherical enlargement of a part or of the whole of the ductus choledochus. This cystic portion may involve only the common duct proper, or may be large enough to include the junction of the cystic, hepatic, and common ducts. Thus, there may be only one duct entering the cyst (the upper part of the common duct), or the hepatic and cystic ducts may enter the "cyst" separately and their orifices may be 2 or 3 cm. apart (Fig. 1). In either instance, the cyst is connected to the duodenum by the lower portion of the common duct. In the cases of Seeliger and Mayesima the enlargement in-

volved such a low portion of the common duct that the pancreatic duct opened directly into the choledochal cyst.

This localized dilatation of the biliary system is unique and is to be differentiated from enlargements which obtain in purely obstructive lesions of the lower common duct, such as those found with carcinoma at the head of the pancreas in the adult. Dilatations which result solely from obstruction tend to be diffuse and affect the entire biliary tree, and in such enlargements the common duct is seldom larger than the diameter of the small intestine. Also, in these obstructive lesions, the gallbladder is markedly dilated. Contrary to such conditions, a true choledochus cyst represents an extreme localized dilatation, primarily in the common duct, and the gallbladder is but little affected.

The dimensions of a cyst may reach large proportions, especially when one considers the size of the patient in which the abnormality may exist. Many of the cysts have had a capacity of one to two liters, and frequently they are described as being the size of a "fist," or the "size of a child's head." That found by Heiliger in a 40 cm. fetus was 3 cm. long and 2½ cm. in diameter. There is little relationship between the duration of symptoms and the size of the cyst; thus, in Bolle's case with symptoms of only two weeks' duration, the cyst was "larger than a man's head," while Krabbel's patient with complaints for eight years, had a cyst "the size of a fist." There is no constant correlation between the size of the cyst and the age of the patient, although the largest cysts tend to be found in older patients.

The cyst wall is often quite firm and may vary from 2 to 3 or even 4 mm. in thickness. This heavy wall is usually composed of a dense connective tissue in which elastic tissue and smooth muscle elements are often lacking. The lining of the cyst rarely contains any epithelium, and the inner surface is usually represented by a heavy layer of connective tissue. The inner surface may be roughened and irregular, may be covered by heavy deposits of bile pigments, and occasionally the presence of purulent exudate is indicative of infection within the cyst. Microscopically, the cyst wall generally shows evidence of extensive inflammatory reaction.

Valve-like folds within the cyst are described by various authors. These are thin flaps of tissue which, when present, are adjacent to the openings of the ducts. These flaps have been found at least five times near the cyst exit, twice adjacent to the hepatic duct opening, and once in the region of the cystic duct opening. Such a valve may be several millimeters in thickness, and, though irregular in outline, may have dimensions as large as 1.5 by 2 cm.

The lower portion of the common bile duct may present a variety of conditions. Thus, very large cysts may lie immediately against the duodenum in the region of the ampulla of Vater and leave only a few

millimeters of normal duct joining the cyst to the intestine. Contrary to this, the cystic dilatation may involve only the upper section of the common duct and thus leave several centimeters of normal duct joining the cyst and duodenum. In 6 cases a note was made that this lower part of the duct was angulated, and yet in all of these cases the duct could be probed. The lower part of the duct was stenosed in 7 instances, but in another case there was an abnormally large opening into the duodenum.

No opening from the cyst to the duodenum could be found in the following cases: At the times of operation, Erdély and Weiss could find no exit. Ashby reported that the common duct was obliterated near the duodenum, and similarly, Arnolds and Rolleston found no openings from the cysts. At postmortem examination, Giezendanner found only a small band of connective tissue running downward toward the intestine. Wyllie, also, could not demonstrate a cyst outlet at autopsy. Lavenson found 1 cm. of the lower part of the common duct to be normal before entering the duodenal wall, but the intramural portion was 2 cm. long and was entirely devoid of lumen; microscopic examination of this latter part revealed extensive fibrosis with complete obliteration of the lumen and disappearance of all traces of epithelial elements. Such obliteration of the exit, however, is probably inflammatory in origin. That such atresia is not congenital is shown by the period of months or years during which each of these patients had been free of jaundice prior to the onset of symptoms. It is possible that such obliteration of the exit may be the result of an inflammatory process superimposed on a congenital stenosis of the lower part of the common duct.

The cystic duct, hepatic duct, and gallbladder may exhibit a minor degree of dilatation due to partial or complete obstruction to biliary flow, but such changes are unimportant when compared to the size of the common duct.

The liver is usually enlarged. In Heid's patient, a fourteen-year-old girl, the organ weighed 3035 grams. Cirrhosis is frequent and this condition imparts a firm or hard consistency and a fine pebbly surface to the liver. In a minority of cases the intrahepatic ducts are grossly dilated. Microscopically, there is often a cirrhosis with increased periportal connective tissue, proliferation of the bile capillaries, and rarely some bile stasis. Infection is common, and leucocytic infiltration of the portal areas may be marked. Cholangitis may reach an advanced stage, and intraductal suppuration has been seen.

Displacement of the abdominal viscera is due to the presence of the cyst and the enlargement of the liver. Thus there may be a downward, medial, and forward displacement of the first and second portions of the duodenum, so that this part of the intestine lies flattened out on the anteromedial surface of the cyst.

ETIOLOGY

Many hypotheses have been advanced regarding the underlying cause for the production of this malady and the following include the views of leading authors.

1. An anomalous direction of the common duct through the duodenal wall forms a kink in the duct which produces obstruction to biliary flow. (Rostowzew and Waller.) Such obstruction is thought to be the causative factor in common duct enlargement.

2. A congenital stenosis of the lower part of the common duct causes back pressure sufficient to produce dilatation. (Edgeworth and Ladd.)

3. The dilatation may be due to an achalazia, namely, a failure of Oddi's sphincter to relax at the proper time, which causes obstruction by neuromuscular incoordination. (Rolleston.)

4. The cyst represents a developmental anomaly which is present before birth, and is primarily due to a weakness of the common duct wall which allows dilatation under normal intraductal pressure. (Heiliger.) The condition has been compared to a congenital idiopathic hydronephrosis, and, similar to this renal condition, there may be no demonstrable obstruction. (Bohmanson.)

5. The common duct wall lacks contractile elements and balloons out locally following obstruction in the lower portion of the duct. (Ebner, Schloessman, Seeliger, Arnolds, and Bolle.) Dreesman supports this theory and specifies the obstruction to be by valve formation from redundant lining membrane of the duct secondary to cholangitis. Lavenson and Ashby also postulate the congenital weakness of the duct wall, but believe the obstruction to be due to fibrosis of the lower part of the duct from cholangitis.

6. The cyst is of "congenital origin" and represents a malformation of the duct, while the valve formation is entirely secondary. Thus, as a cyst enlarges and displaces downward (because of its size and weight), an angulation forms which may lead to valve formation. (Giezendanner.) Such valves, after they are once formed, may give obstruction and aggravate the symptoms, but they are not the primary cause of cystic dilatation.

7. Primarily, there is an enlarged duct which causes no symptoms until it gets infected and also gets obstructed by cholangitis. (Zipf.) Hence a patient may have many years of normal life before symptoms of choledochus cyst become manifest.

8. The cystic dilatation may arise from an abortive diverticulum from the common duct similar to the diverticulum which gives rise to the ventral pancreas. (Winternitz.)

9. Pancreatic rests in the common duct wall weaken it and allow local dilatation. An analogy is thus drawn to diverticuli of the duodenum which frequently contain rests of pancreatic tissue. (Budde.)

10. Common duct cysts may be derived from accessory gallbladder formations which are outpocketings from the common duct. (Budde

and Erdély.) Such rudimentary and additional duct buds are common in human embryos and may spring from any one of the three primary ducts, but more frequently do so at the junction of all three. (Keibel and Mall.) The persistence of one of these small outpocketings could conceivably result in formation of a choledochus cyst.

With such a multiplicity of explanations it is entirely possible that we are dealing with a heterogeneous group of cases which may be produced in several ways, for while many of the theories are plausible, no one explanation fulfills the conditions found in all clinical cases. In review, the most feasible theory is that which accepts a congenital weakness of the duct wall, but which defect does not produce dilatation unless there is a second factor of obstruction with resultant increased intraductal pressure. Such obstruction in various cases has been caused by duct angulation, valve formation, inflammation, or by stenosis of the lower portion of the common duct.

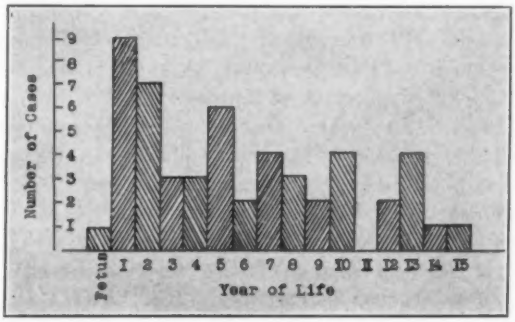

Fig. 5.—Ages of patients at onset of choledochus cyst symptoms. The number of patients in each age group is indicated by the height of the columns. One case occurring in a fetus is also indicated.

AGE INCIDENCE

In Fig. 5 an attempt is made to list the patients at the ages at which symptoms were first noticed.

SEX INCIDENCE

Of these 52 cases in childhood, 13 occurred in males and 39 in females. The condition, therefore, is approximately three times more common in females than in males, but the series is too small to permit any conclusions in regard to sex distribution.

SYMPTOMS AND SIGNS

The outstanding feature of the symptoms and signs of choledochus cyst in childhood is the triad of abdominal pain, abdominal tumor, and jaundice.

Pain is stated to have been present in 33 cases, absent in 4 cases, and questionable in 1. Of the 14 remaining cases, 1 was a fetus, and 13 do not mention pain as a complaint. Thus, the incidence of this

symptom is at least 63 per cent, and this figure would probably be higher if more complete data were available. Pain is usually located in the epigastrium or in the right upper quadrant of the abdomen, but in 3 instances was noted to be about the umbilicus. In 6 cases it was described as colicky, but more often it is of a "dragging" nature, or is described as pressure or discomfort from the abdominal mass. The pain is usually not very severe, and while it may cause considerable discomfort, it is rarely sufficient to make the patient "double up" or cry out. Pain is occasionally accompanied by nausea, but vomiting has occurred in only a few instances. As previous authors have noted, there is no correlation between the size of the cyst and the severity of the pain.

Abdominal tumor was stated to be present in 45 cases, but in one of these cases the tumor was felt only after etherization of the patient. In 1 case no tumor was felt, and in the 6 remaining cases no information is available regarding the presence or absence of abdominal swelling. Hence, the presence of an intraabdominal mass, either as given in the history or as found by physical examination, was detected in at least 87 per cent of the cases.

In about half of the cases a well-defined and circumscribed mass could be palpated just below the liver edge, but in other instances it is described as producing only a resistance to palpation of the right upper quadrant. In 5 cases the abdominal enlargement was generalized and no local swelling could be discerned in the liver region. When the cyst can be felt, it is often farther to the left than might be expected, for, because of its size and because of the associated large liver, the dilated common duct may extend over the midline of the body and may even be noted as a mass in the umbilical region. In 10 cases the mass was designated as "definitely cystic," "elastic," "tensely cystic," or some such term which indicated its true nature, but not infrequently the cyst has been so tense that it has been described as firm or solid. Hence, the mass may give the impression that it represents a neoplasm or an enlarged lobe of the liver.

The size and tenseness of the cyst may vary from time to time in proportion to obstruction at the cyst outlet or with quantitative changes in the production of bile after the ingestion of food. Schloessman and Morley both noted that the size of the cysts in their cases receded without treatment. The abdominal mass in Taylor's case appeared intermittently and was always present the day after attacks of pain and vomiting. Giezendanner, Rostowzew, Heid, Smit, Waller, and Wettwer mentioned great variations in size and consistency on different occasions and called attention to these peculiar and striking changes. In the second case here reported, frequent abdominal palpation gave the impression that the mass varied in size and tension. It is quite likely that this is a sign which has been present more often

than recorded, for the symptom complex as a whole often has an intermittent character and the intermittent biliary obstruction (as shown by recurring jaundice) probably produces considerable changes in the size and tenseness of the choledochus cyst.

The cyst may or may not move during respiratory movements of the diaphragm. Of 18 cases for which such data are recorded, 9 did move during respiration and 9 did not. While palpation of the cyst usually causes no discomfort, 5 patients did complain of local tenderness.

Jaundice is a prominent symptom and was present in 43 cases—an incidence of at least 83 per cent. It was questionable in 1 case, absent in 4, and not mentioned in 4. The stools were acholic in 19 instances, were normally colored in 8, and were not mentioned in the remaining cases. Biliary pigments were present in the urine in 10 patients.

Fever was present in 10 patients, and is probably a reflection of cholangitis or hepatitis. The fever range was up to 101° or 102°, but in one case was up to 104.4°.

The sequence of onset of pain, tumor, and jaundice, etc., may vary in different cases. Thus, any one of these symptoms may occur first, may exist alone, or may persist in combination with other symptoms. One symptom may be present for a long period of time before the onset of others.

The duration of symptoms before the condition is recognized varies over a wide range, but the possible chronicity of complaints is noteworthy. The average duration of symptoms was about three years (not counting the patients of McWhorter, Fenger, and Dreesman whose illnesses were exceptionally long). The severity of symptoms bears no constant relationship to the duration of complaints.

The intermittency of symptoms should be emphasized. When it is stated that symptoms are "intermittent," it is meant that the general course of the illness has been one of exacerbations and remissions. Though one or more of the symptoms were persistent, 25 cases had definite intermittency of one or more symptoms, while in 9 instances the symptoms were entirely of a progressive nature. Of the remaining 18 cases it is impossible to determine how the course of illness was characterized.

X-ray studies give but little additional information. In one case the cyst was faintly outlined by opaque substance which had been given for gallbladder studies. With barium meal studies of the gastrointestinal tract, the duodenum and stomach have been seen to be displaced forward, downward, and to the left (by the cyst).

DIAGNOSIS

The history and physical findings are usually typical and should practically exclude most of the errors in diagnosis which have previously been made. In reviewing the individual cases reported, the

impression is gained that a correct diagnosis could often have been ventured had the possibility of idiopathic choledochus cyst been entertained as a cause of the patient's complaints. Yet the diagnosis of choledochus cyst has been made preoperatively only 3 times in this series of cases occurring in childhood—in Taylor's, Erdély's, and in the first case here reported.

TABLE I

DIAGNOSES MADE IN 52 CASES OF CHOLEDOCHUS CYST IN CHILDHOOD

No diagnosis (or none stated)	20
Echinococcus cyst	12
"Exploratory laparotomy"	3
Abdominal neoplasm	3
Congenital choledochus cyst	3
Stone in common duct	2
Tuberculosis	1
Cholangitis	1
Obstruction to common duct by worms	1
Cyst of the liver	1
Cholecystitis	1
Cholecystitis and cholelithiasis	1
Hydrops of the gallbladder	1
Intestinal obstruction	1
Congenital abnormality of the bile ducts	1
Liver abscess	1

DIFFERENTIAL DIAGNOSIS

Echinococcus cyst of the liver has symptoms and physical findings similar to those of choledochus cyst, but more often is characterized as a palpable tumor of the liver which causes little disturbance to the patient's health. The tumor is usually of long standing and is the only complaint; but if suppuration occurs, there are additional indications of infection, and if the tumor is very large, there may be associated jaundice. The cyst of echinococcus is stationary or progressive in size, whereas the choledochus cyst may vary in size, especially following the ingestion of food. A hydatid cyst of the liver moves with respiration and rarely produces pain. The presence of echinococcus cysts in other organs is of aid in detecting the parasitic disease. The geographic location of the patient in countries where the disease is rare, the absence of these parasites in dogs of the community, and the lack of intimate contact with dogs, all tend to exclude echinococcus cysts as a probable diagnosis. Where facilities are available, negative complement fixation tests or precipitation reactions should rule out the possibility of echinococcus infection.

Cholelithiasis is very rare in children and its exclusion should be made with ease. X-ray studies may give aid in indicating the presence of stones.

Abdominal neoplasms in childhood, without treatment, run a rapidly progressive and fatal course. Thus, if a child has had symptoms

from an abdominal mass for a year or more and still maintains fair nutrition and vitality, neoplasm as a causative agent is unlikely. Therefore, when this differential diagnosis is in question, a long duration of symptoms should tend to exclude malignancy.

Congenital cysts of the liver are more apt to be multiple small cysts, rather than one large mass, and they are practically always accompanied by cystic kidneys. The liver involvement is rarely manifest or suspected before adult life, and attention is attracted primarily by the kidney masses.

Congenital atresias of the bile ducts should give no difficulty, chiefly because of the different age groups into which the two classes of patients fall. The average age of patients with congenital atresias of the extrahepatic ducts is from one to three months when first seen. In those cases not amenable to operative relief, the expectancy of life is a matter of a few months. In this series of 52 cases of choledochus cyst, only 9 had any symptoms before one year of age, and only 5 of these had any symptoms before six months of age. Of these 5 cases, 3 were aged four, eight, and eight years, respectively, when first seen, and hence the duration of life completely excluded congenital atresia of the bile ducts as a diagnosis. Thus, the older age group incidence of choledochus cyst sharply differentiates the two conditions.

Pancreatic cysts at the head of that organ, producing pressure on the common bile duct, can simulate idiopathic cyst of the common duct so closely that a differential diagnosis may be impossible. The position of a pancreatic cyst, however, tends to be more to the left than that expected for tumor of an enlarged bile duct. A pancreatic cyst, in addition, is stationary or progressive in size, whereas the common duct dilatation may show variations in size and tenseness.

TREATMENTS AND RESULTS

In 42 cases it is reasonably certain when the correct diagnosis was made. In Table II these 42 cases are listed to show the relationship between the time of making a correct diagnosis and the final outcome of a given case. Of the 11 cases discovered at autopsy, at least 4 had been operated upon and the condition not recognized.

TABLE II

FORTY-TWO CASES IN WHICH THE TIME OF MAKING THE CORRECT DIAGNOSIS IS KNOWN

CORRECT DIAGNOSIS MADE	RECOVERED	DIED
Preoperatively	3	0
At first operation	11	12
After first operation	0	3
At second operation	1	2
At autopsy	–	11

The 23 cases in which the correct diagnosis was made at first operation may be grouped as: (1) those which were treated by the accepted method of primary anastomosis of the biliary system and intestine, and (2) those which were treated by other procedures. (Table III.)

TABLE III

DIAGNOSIS MADE AT FIRST OPERATION—23 CASES

TREATED BY PRIMARY ANASTOMOSIS OF BILIARY SYSTEM AND INTESTINE		TREATED BY OTHER PROCEDURES	
RECOVERED	DIED	RECOVERED	DIED
7	1	4	11

Thus, even if the diagnosis is not made preoperatively, the probabilities of a cure are high if the condition is recognized at the first operation and proper treatment is immediately instituted.

The types of treatment and the respective end-results are summed up in Table IV.

TABLE IV

TREATMENT	DIED	RECOVERED
1. No operation	9	0
2. Type of operation not stated	1	0
3. External drainage of the biliary system		
A. Drainage of choledochus cyst	15	1
B. Drainage of gallbladder	1	0
C. Drainage of hepatic duct and excision of cyst	3	0
D. Drainage of gallbladder and excision of cyst	1	0
4. Drainage of cyst at first operation and anastomosis to intestine at second operation	5	5
5. Anastomosis of biliary system and intestine at one operation		
A. Hepaticoenterostomy with cholecystectomy and excision of choledochus cyst	0	1
B. Cholecystenterostomy	0	2
C. Choledochoenterostomy	1	7
	36	16

1.—All patients who were not operated upon died. In all of these cases, the cyst was discovered at autopsy. At least 6 of these patients had had symptoms before death, while in 2 the antemortem course is not stated, the ninth being found in a fetus.

2.—In 1 case the type of operation was not stated; outcome was fatal.

3*A*.—Of the 16 patients who had only an external drainage of the cyst performed, 15 died. Included in this group of 15, there is 1 case in which drainage of the cyst produced a biliary fistula, and closure of this fistula two months later at a second operation resulted in death. Of the 15 patients who died following external drainage of the cyst, 1 died in nine days, another in twenty-two days, and 4 lived

one to three months before succumbing; hence there is a possibility that recovery might have been secured in these last 6 cases had secondary operation been performed for anastomosis of the cyst and intestinal tract. The sixteenth case (which was treated only by external drainage of the cyst) had a choledochostomy and sustained a biliary fistula for two months. Following the spontaneous closure of this fistula there was a return of symptoms, and a second drainage of the cyst led to another fistula which persisted for five weeks and then closed over spontaneously. At a third operation, the cyst was found shrunken to the size of a walnut and no further procedure was undertaken. This patient was well four years later, and represents the only case cured by external drainage alone.

3*B*.—With equally discouraging result, a cholecystostomy was performed in one case, with a fatal outcome in one day.

3*C*.—Excision of the cyst and external drainage of the hepatic duct was uniformly fatal, though one patient lived for three months after operation and probably warranted a secondary attempt for directing the flow of bile into the intestine.

3*D*.—In one case, the removal of the cyst with establishment of a cholecystostomy to drain the biliary system resulted in death in three days.

4.—Ten cases were treated by external drainage of the cyst at a first operation and with anastomosis of the cyst and intestine at a second operation. Five of these died and five survived. The interval between the two operations bore no relationship to the end-results, for of those who died, the second procedure was performed sixteen days, ten weeks, three months, and two months, respectively, after the first operation (and the time was not mentioned in the fifth case). Of those who recovered, the second operation was done four months, two days, three months, three months, and three weeks later. Two patients in this series of 10 cases had incidental cholecystectomy, one being performed at a first operation and the other at the second operation; and both patients lived. One of the cases in this series of 10 had a third operation because the choledochoenterostomy was not functioning well; and a choledochogastrostomy performed at this third sitting led to successful result. Two patients in this series had abdominal taps preoperatively; one for diagnostic purposes, and the other for relief of symptoms (tapped 10 times over a period of three months).

5-*A*, *B*, and *C*.—Without doubt, the treatment of choice is to perform a primary anastomosis between the biliary system and the intestinal tract at one operation. Of the 11 cases thus treated 10 recovered. Two of the successful cases had anastomoses between the gallbladder and duodenum. But by far, the treatment which merits most credit is that by which the cyst is joined to the duodenum, 7 of 8 patients thus treated having survived. In 2 of these successful cases, a chole-

TABLE V

FIFTY-TWO CASES OF CHOLEDOCHUS CYST IN CHILDHOOD

NUMBER	YEAR	AUTHOR	AGE (IN YR.) AND SEX	PAIN	TUMOR	JAUNDICE	ACHOLIC STOOLS	SYMPTOMS INTERMITTENT	SYMPTOMS DURATION	PREOPERATIVE DIAGNOSIS	CORRECT DIAGNOSIS MADE AT	SIZE OF CHOLEDOCHUS CYST	TREATMENT	RESULT
1	1893	Heid	14 F	6 wk.	6 wk.	6 wk.	–	–	6 wk.	?	Autopsy	18 × 13 × 14 cm.	No operation	Died of diphtheria and erysipelas
2	1895	Edgeworth	4 F	–	1 yr.	Attacks since 6 mo. of age	–	+	Since 6 mo. of age	Recurrent Cholangitis	Autopsy	29 oz. bile removed at operation	Choledochostomy	Died one week after operation
3	1896	Fenger	33 F	+	+	+	+	+	Since 8 yr. of age	Stone in common duct	Operation	Size of a hen's egg	Cholecystostomy, with exploration of cyst and duodenum	Died 24 hours after operation
4	1897	Broca	10 F	–	+	Slight	–	–	–	Generalized tbc.	Autopsy	?	No operation	Died from generalized tbc.
5	1897	Brun and Hartman	3 F	?	+	0	–	0	15 days	Echinococcus cyst	(?) First operation	?	1st op. choledochostomy. 2nd op. 4 mo. later — choledochoenterostomy	Recovered
6	1897	Russell	8 M	4 days	3 days	4 days	+	0	5 days	Echinococcus cyst	After operation	?	Choledochostomy	Died 4 days after operation
7	1898	Ashby	7 F	–	+	2½ yr.	+	–	2½ yr.	?	(?) First operation	–	Aspirated 10 times in 3 mo. Then 1st op. —choledochostomy. 2nd op.—2 mo. later—attempted choledochoenterostomy	Died day after operation

TABLE V—CONT'D

8	1899	Nicholaysen	8 F	0	+	3 mo.	–	+	1 year	?	?	17 cm. long 15 cm. wide	1st op. packing against cyst. 2nd op.—6 days later—choledochostomy	Died day after operation Probably chloroform death
9	1902	Rostowzew	13 F	3 wk.	3 yr.	+	0	3 attacks of icterus	3 yr.	Echinococcus cyst	Operation	2 liters capacity	Choledochostomy	Died day after operation
10	1905	Kolb	10 F	–	Several mo.	Several mo.	–	–	Several mo.	Echinococcus cyst	? Operation	1½ liters capacity	Diagnostic aspiration. Op.—2 wk. later—choledochostomy	Died about 1 mo. after operation
11	1905	Rolleston	9 F	–	–	–	–	–	–	?	? Autopsy	"Size of a fist"	No operation	Died
12	1905	Wettwer	15 F	10 yr.	+	8 yr.	–	Icterus intermittent	10 yr.	?	Autopsy	"Twice the size of a fist"	No operation	Died
13	1906	Arnolds	13 F	+	+	2 mo.	+ ?	–	Sickly for 11 yr. Definite symptoms 2 mo.	? Echinococcus cyst. ? Neoplasm	After operation	"Large as a man's head"	Choledochostomy	Died 1 day after operation
14	1906	Dreesman	24 F	+	+	Attacks since 6 mo. of age	+	+	23½ yr.	Echinococcus cyst	After 1st operation	"Size of a child's head"	1st op. cholecystostomy and choledochostomy. 2nd op. 3 mo. later. Choledochoduodenostomy	Died 3 days after operation
15	1909	Ebner	18 F	Began at 9 yr.	+	6 mo.	0 ?	+	9 yr.	? Echinococcus cyst. ? Hepatic cyst	? Operation	2 liters of bile removed at operation	Choledochostomy	Died 3 mo. later of bleeding. Purpura unassociated with jaundice

TABLE V—CONT'D

NUMBER	YEAR	AUTHOR	AGE (IN YR.) AND SEX	PAIN	TUMOR	JAUNDICE	ACHOLIC STOOLS	SYMPTOMS INTERMITTENT	SYMPTOMS DURATION	PREOPERATIVE DIAGNOSIS	CORRECT DIAGNOSIS MADE AT	SIZE OF CHOLEDOCHUS CYST	TREATMENT	RESULT
16	1909	Lavenson	8 F	0	3 wk.	1 yr.	8 mo.	0	1 yr.	?	Operation	15 × 8 × 7 cm.	Cholecystostomy with removal of choledochus cyst	Died 3 days after operation
17	1909	Weiss	6 M	+	6 mo.	+	+	+	14 mo.	Echinococcus cyst	Autopsy	"Fist size"	Diagnostic abdominal tap. Then 1st op.—suture of cyst to abdominal wall. 2nd op.—3 days later—opening of cyst	Died 9 days after operation
18	1910	Butters	5 M	–	+	+	–	–	–	?	–	3 liters capacity	External drainage	Died several days after operation
19	1910	Heiliger	40 cm. fetus M	–	–	0	–	–	–	–	Autopsy	3 cm. long 2½ cm. wide	–	Died
20	1911	Schloessman	7 F	2½ wk.	+	+	0	0	2½ wk.	Hepatic cyst	Operation	"Size of a child's head"	Aspiration and choledochostomy	Died 6 days after operation
21	1912	Mayesima	2 M	–	10 mo.	4 mo.	0	–	10 mo.	?	–	2100 c.c. of bile aspirated	Aspiration followed by choledochostomy	Died 2 mo. after operation

TABLE V—CONT'D

22	1913	Rotgans	5 F	+	0	+	–	Jaundice intermittent	–	Cholecystitis	–	–	1st op.—cholecystectomy and choledochostomy. 2nd op. 4 mo. later—choledochoduodenostomy	Recovered
23	1914	Roberts	2 F	0	+	+	–	–	–	?	–	–	External drainage	Died 1 wk. after operation
24	1916	Seeliger	13 F	+	1 mo.	1 mo.	0	0	1 mo.	? Echinococcus cyst. (?) Perforated cholecystitis	2nd operation	750 c.c. of bile aspirated from cyst at operation	1st. op.—sewed cyst to abdominal wall and opened it next day. 2nd op.—16 days later—choledochoenterostomy	Died 6 days after operation
25	1917	Waller	10 F	7 yr.	+	Slight	0	+	7 yr.	None	Operation	200 c.c. capacity	Choledochoduodenostomy	Recovered
26	1920	MacConnell	11 F	1 yr.	6 mo.	Slight	–	–	1 yr.	?	1st operation	Over a pint of bile removed at operation	1st. op.—choledochostomy (drained 2 mo.). 2nd op.—10 mo. later—choledochostomy (drained 5 wk.) 3rd op.—3 yr. later—cyst had shrunk to walnut size—nothing done	Recovered
27	1921	Schürholz	3 F	6 wk.	+	+	–	–	6 wk.	? Echinococcus cyst	1st operation	"Size of a child's head"	1st op.—choledochostomy. 2nd op.—10 wk. later—choledochoenterostomy	Died 3 hr. after operation
28	1921	Yamanouchi	4 F	+	+	+	–	–	–	?	–	"Size of a child's head"	Type of operation not stated	Died

TABLE V—CONT'D

NUMBER	YEAR	AUTHOR	AGE (IN YR.) AND SEX	PAIN	TUMOR	JAUNDICE	ACHOLIC STOOLS	SYMPTOMS INTERMITTENT	SYMPTOMS DURATION	PREOPERATIVE DIAGNOSIS	CORRECT DIAGNOSIS MADE AT	SIZE OF CHOLEDOCHUS CYST	TREATMENT	RESULT
29	1922	Bolle	13 F	+	+	Marked	+	Several attacks	2 wk.	Echinococcus cyst	2nd operation	"Larger than a man's head"	1st op.—choledochostomy. 2nd op.—3 mo. later—choledochoenterostomy & cholecystectomy	Recovered
30	1922	Zipf	14 F	+	+	Slight	–	0	3 days	?	Operation	"Size of a fist"	External drainage	Died 3 days after operation
31	1923	Morley (Ashby & Platt)	6 F	+	+	+	+	–	Several wk.	Exploratory laparotomy	Operation	–	1st op.—choledochostomy. 2nd op.—2 mo. later—closure of biliary fistula	Died a few hours after operation
32	1924	Bohmansson	3 M	1 yr. and 2 mo. before entry	2 mo.	2 mo.	2 mo.	+	1 yr.	? Retroperitoneal tumor	1st operation	1000 c.c. capacity	1st op.—choledochostomy. 2nd op.—2 days later—choledochoduodenostomy	Recovered
33	1924	Krabbel	8 F	+	Felt only after etherization	From 14 days to 6 mo. of age	+ ?	+	8 yr.	? Echinococcus cyst. ? Hepatic abscess	1st operation	"Size of a fist"	1st op.—choledochostomy. 2nd op.—3 wk. later—cholecystoduodenostomy. 3rd op.—2 yr. later—choledochogastrostomy	Recovered
34	1924	McWhorter	49 F	Attacks since 6 mo. of age	+	From 6 mo. to 7 yr of age	During attacks	+	"From the age of 6 mo."	Common duct stone	Operation	10 cm. long 6 cm. in greatest diameter	Excision of gallbladder and common duct cyst, hepaticoduodenostomy	Recovered

TABLE V—CONT'D

35	1924	Wright	15 M	Mild	+	5 mo.	1 mo.	–	At least 8 mo.	Obstruction of common duct by worms	Operation	"Size of a fetal head"	Choledochoduodenostomy	Died 3 days after operation
36	1925	Ewoyan	6 M	–	–	–	–	–	–	–	–	–	Excision and drainage (?) of hepatic duct	Died 3 mo. after operation
37	1925	Hill & Ramsay	2 F	–	1 mo.	+?– at 9 mo. of age	–	–	At least 1 mo. (?) 13 mo.	Exploratory laparotomy	Autopsy	4 in. in diameter	Choledochostomy	Died 22 days after operation
38	1925	Fothfalussy	12 M	–	–	–	–	–	–	–	–	–	Excision and drainage (?) of hepatic duct	Died
39	1925	Wyllie	6 F	+	1 yr.	1 yr.	+	+	1 yr.	Exploratory laparotomy	1st operation	4 oz. of bile removed at operation	1st op.—choledochostomy. 2nd op.—choledochoduodenostomy	Died 48 hr. after operation
40	1928	Erdély	17 M	+	+	+	–	+	5 yr.	Idiopathic choledochus cyst	Before operation	"Large as a man's fist"	Choledochoduodenostomy	Recovery
41	1928	Feyrter	7 F	–	–	–	–	–	–	Intestinal obstruction	–	9 × 9 × 7 cm.	No operation	Died of septicemia
42	1928	Judd & Greene	13 F	+	+	During 2 attacks	+	+	? 11-12 yr.	Cholecystitis and (?) cholelithiasis	Operation	13 cm. in diameter	Choledochoduodenostomy and cholecystostomy	Recovered
43	1928	Ladd	5 F	+	–	+	–	+	"Since birth"	–	Operation	–	Cholecystoduodenostomy with Murphy button	Recovered
44	1928	Ladd	4 F	Since infancy	+	Marked	+	+	4 yr.	Congenital abnormality of bile ducts	Operation	Filled entire rt. upper abdominal quadrant	Cholecystoduodenostomy	Recovered
45	1928	Taylor	23 F	+	+	+	+	+	"Since she was a small child"	Cystic dilatation of common duct	Before operation	"Size of a tangerine"	Choledochogastrostomy	Recovered

TABLE V—CONT'D

NUMBER	YEAR	AUTHOR	AGE (IN YR.) AND SEX	PAIN	TUMOR	JAUNDICE	ACHOLIC STOOLS	SYMPTOMS INTERMITTENT	SYMPTOMS DURATION	PREOPERATIVE DIAGNOSIS	CORRECT DIAGNOSIS MADE AT	SIZE OF CHOLEDOCHUS CYST	TREATMENT	RESULT
46	1928	Willis	12 M	6 mo.	+	0	0	+	4 yr.	Hydrops of gallbladder	Operation	400 c.c. capacity	Choledochoduodenostomy	Recovered
47	1929	Giezendanner	4 F	3½ mo.	+	Mild	–	+	At least 3½ mo.	–	Autopsy	2 liters capacity	No operation	Died after 3 mo. observation
48	1930	Matthieu	(6 wk.) M?	?	+	+	–	0	4 wk.	–	Autopsy	4½ in. diameter	No operation	Died
49	1930	Terada & Vagi	(4½ mo.) M	–	+	4 mo.	+	0	4 mo.	–	Autopsy	10 × 8 × 5 cm.	No operation	Died
50	1930	Wilson	14 F	+	+	0	–	+	12 yr.	–	Operation	20 cm. in diameter	Choledochoduodenostomy	Recovered
51	1933	Gross	5 F	10 mo.	1 mo.	10 mo.	10 mo.	+	10 mo.	Congenital cyst of the common duct	Before operation	13 cm. in diameter	Choledochoduodenostomy and cholecystostomy	Recovered
52	1933	Gross	3 F	0	1 yr.	Two attacks 1 yr. & 3 wk. before entry	3 wk.	+	1 yr.	? Abdominal neoplasm	2nd operation	12 cm. long 7 cm. in diameter	1st op.—biopsy of liver (thought to contain neoplasm). 2nd op.—6 wk. later—excision of cyst and drainage of hepatic duct	Died 7 hr. after operation

cystostomy was performed in addition as a safety outlet to relieve tension from the sutures of the anastomosis. While this extra step was performed only by Judd and Greene and by Ladd in the first case here reported, it doubtless should be accepted as an additional safety producing factor.

Excision of the cyst should never be attempted, for it is unnecessary and is productive of dangerous surgical shock. There has been ample opportunity to demonstrate the potentiality of the cyst to shrink to small dimensions when adequate drainage is instituted.

Abdominal tapping is to be avoided, because of the danger of producing a leak from the cyst into the abdominal cavity, and also because of the possible injury to other viscera.

The mortality in the entire group of 52 patients was 69 per cent, but in those cases treated by primary anastomosis between the biliary and intestinal systems the mortality was 9 per cent.

SUMMARY

Fifty-two cases of idiopathic choledochus cyst in childhood are reviewed. Two of these cases are reported for the first time.

The more important symptoms and signs are usually characteristic and consist of abdominal pain, abdominal tumor, and jaundice. The size and tenseness of the abdominal tumor in a given case may vary from time to time. Acholic stools may be present and there may be bile in the urine. The average duration of symptoms was about three years. In approximately one-half of the cases the symptoms had been intermittent and had occurred in attacks with intervening periods of remission. About three-fourths of the patients were females. The correct diagnosis was made only three times before operation, but the nature of the history and the physical findings should enable the diagnosis to be made more frequently.

The important pathologic finding is a large cystic dilatation of the common duct. In one-half of the cases there was an angulation, stenosis, obliteration, or valve formation at the cyst outlet, but many of these conditions were probably the result of rather than the cause of the common duct enlargement. The liver was practically always enlarged and biliary cirrhosis and cholangitis were common.

The etiology of the condition has not been definitely determined, but many theories have been advanced. The common duct dilatation is most likely a result of congenital weakness of the duct wall which is not productive of enlargement until there is obstruction to the flow of bile. Such obstruction may be from congenital stenosis, valve formation, angulation, or cholangitis of the lower common duct.

The accepted form of treatment is to anastomose the biliary and the intestinal tracts at one operation, the most acceptable method of doing this being the production of a choledochoduodenostomy.

The mortality in the entire group of 52 patients was 69 per cent, but in those treated by primary anastomosis of biliary tract and intestine the mortality was 9 per cent.

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VULVOVAGINAL DIPHTHERIA

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THE picture of diphtheritic vulvitis and vulvovaginitis has been known for many years through the classical descriptions by Herard and Trousseau. It is, however, a rare form among the various diphtheritic infections, and the occurrence of such a case at Kingston Avenue Hospital prompted this report.

Diphtheroid bacilli are commonly found vegetating on the surface of the human skin and on the lining membranes of various body cavities. The report of Hewlett[1] in the Medical Research Council of London states that the group as a whole is singularly devoid of pathogenic properties. Although cases of diphtheria of the genital organs due to virulent bacilli do occur, no instance is known in which the identity has been completely established. Only a few of the reported cases of vaginal diphtheria mention any confirmatory cultures and virulence tests.

Vaginal cultures were taken on the maternity wards in several clinics, with varying percentages of diphtheria bacilli reported.[2] Broer, in 1919, found 23 per cent, Lietz, in 1920, 14.2 per cent, and Wauschkuhn, in 1920, 5.5 per cent. Lönne and Schugt[3] studied 300 cases, using both direct smear and culture, and reported no true diphtheria bacilli in a single instance. They found, however, a pseudodiphtheria organism in 45 per cent of the smears.

Contrary to the statement of Ker[4] in his textbook that the vulva is a comparatively common site for diphtheria, either primary or secondary, a careful search of the literature does not warrant so sweeping a remark. Lee and van Saun[5] state that for thirty years prior to 1922 only 26 cases were reported, 6 possibly primary, the others secondary to diphtheria of the nose or throat. They add, further, that since 1922 only six references to diphtheritic vaginitis in children were noted, and report a case of primary origin.

Baginsky,[6] in 1913, found only 2 or 3 cases among almost 300 patients, and remarked that the disease was dangerous. Szirmai[7] in Budapest, with 1122 diphtheria patients over a period of nine years, reported 10 cases, of which 9 were primary and one was secondary. Von Kiss[8] completed the Budapest series up to 1930, with 429 more patients and only one case of vulvovaginal diphtheria, totaling 11 cases among 1551 patients, or an incidence of 0.7 per cent.

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Mason[9] reported a primary vaginal infection in a girl who had a paronychia of the finger two weeks previously, but had also been exposed to a sister with a sanguineous nasal discharge. Stammer's case[10] was secondary to nasal diphtheria. Von Kiss recently reported a case of primary vaginal diphtheria with subsequent fatality due to a severe myocardial degeneration, as evidenced at autopsy. Benthin[11] found two cases of nonmechanically caused ulcers of the introitus and vagina due to diphtheria bacilli.

Most observers are agreed as to the rarity of the infection, but opinions vary greatly as to the mode of origin. One school claims that the majority of cases of vulvovaginal diphtheria are primary, the other that it is always secondary.

The first group is led by J. von Bókay who states that in the Budapest series 10 of the 11 cases were primary, with no other demonstrable diphtheritic infection present, nor any known previous focus. He mentions 6 additional children with positive vaginal smears but without vulvovaginitis or clinical evidence of a membrane. Transmission to exposed persons was noted in two cases.

Hand transmission is the cause of vulvovaginal diphtheria according to Marfan and Boulanger-Pilet of the second school, and is carried from another part of the body. Baginsky and von Kiss state that it may be primary, but is usually secondary.

The clinical picture of vulvovaginal diphtheria varies from a mild infection to one of a severe nature with cutaneous gangrene. A gray or yellowish gray membrane may form on the inner surfaces of the labia majora and minora, penetrate into the vagina, cross the perineum, and extend down to the anus and rectum. All the tissues involved are red, swollen, and extremely painful. A fetid vaginal discharge may be present, and the inguinal glands are swollen and tender. Small ulcerations may remain for some time after the disappearance of the membrane and in some cases be so deep as to cause loss of substance. A single main symptom common to all cases is a marked dysuria, the pain being so severe that micturition has been voluntarily repressed for fear of pain. Discomfort and pain are also present on walking or moving the legs. There may be no fever or any other concomitant complaint.

Diphtheritic vulvovaginitis is far from being mild both as to outcome or complications. In the eleven-year period of the Budapest series, the mortality among this type was 20 per cent, while over a parallel eight-year period only 12.3 per cent died of other diphtheritic infections. Vasile[12] reported a case of diphtheria of the nose, throat and vagina with death supervening in twenty-four hours.

Postdiphtheritic paralyses have been noted following diphtheritic vaginitis. Ware's case[13] developed a soft palate weakness, Pape[14] reported pupillary paresis, Leenderzt[15] found bladder and rectal incon-

tinence in addition to nasopalatine and extraocular palsy, and von Kiss reported myocardial degeneration with fatal outcome. From the gynecologic services[16] several cases of severe vaginal diphtheria were noted postoperatively, one complicating a pharyngeal diphtheria with a resulting diphtheritic vaginal necrosis. A second woman was infected during her puerperium by one of her other children, and died subsequently. Among other findings Hirsch reported marked vaginal bleeding.

CASE REPORT

A. E., female, aged seven years, was admitted to Kingston Avenue Hospital on the service of Dr. M. B. Gordon, on October 19, 1932, with a history of a sore throat five days previously, and painful urination for the past seven days. She had a slight temperature, but no hoarseness, vomiting, or pain on swallowing. She was not seen by a physician until the day of admission. One week previously she had a cold and a red throat which subsided. She had never received toxin-antitoxin. There are no other children in the family except for a two-and-a-half-year-old cousin who is perfectly well.

Physical examination on admission revealed: temperature 101° F., pulse 130, respirations 20. A whitish yellow, tenacious membrane covered both tonsils which were hypertrophied. No membrane was present in the nose. Bilateral cervical adenitis was present. Heart and lungs were both normal. The vaginal introitus and surrounding tissues were inflamed, violaceous in color, and tender to the touch. A dirty white membrane covered the labia majora and labia minora, the latter being glued together. The clitoris and urethral meatus were red and swollen. The membrane took on a dirty, greenish color as it crossed the perineum toward the anus.

The clinical diagnosis was tonsillar, vulvovaginal, and anorectal diphtheria. The patient received 20,000 units of diphtheria antitoxin intramuscularly and 10,000 units intravenously. Repeated cultures from the involved areas—nose, throat, vulva, vagina, and anorectal region—were all positive for diphtheria. Sugar fermentation with acid production was obtained in dextrose serum-water media but not in saccharose, thus differentiating it from *B. xerosis* and *B. Hoffmanni*.

Blood count: red cells, 4,700,000; hemoglobin, 80 per cent; white cells, 14,500; polymorphonuclears, 82 per cent; lymphocytes, 15 per cent; eosinophiles, 2 per cent; and metamyelocytes, 1 per cent. The urine showed albumin, white cells, and epithelial cells.

The course was rather mild, the temperature dropped to 100° the day after admission and remained so for over three weeks when a temperature of 102° F. developed, due to an injected pharynx and a moderate cervical adenitis. The pulse of 130 dropped gradually to 84 over a three-day period and rose to 140 at the time of the pharyngitis.

The membrane in the throat gradually subsided as did that of the vulval region, but a marked redness of the anorectal region persisted for four days. After the third day the greater part of the membrane had disappeared from the genitalia, except for a small white patch on the right labia minora. This sloughed off gradually, leaving a small defect in the mucosa.

The patient was discharged on the thirtieth day of illness with negative cultures.

Anogenital involvement in the male is quite rare, with lesions of the glans or in a circumcision fold being reported. Anorectal lesions are

usually due to an extension of the membrane across the perineum from a vaginal diphtheria, as in our case.

Cutaneous diphtheria may be found in any part of the body, usually secondary and most always developing on some area of the skin where the epidermis has been injured. Thus we see lesions on the fingers of children from sucking, of persons doing intubations, and pathologists from doing autopsies, all of which clear up rapidly after serum injection.[17] The skin at the root of the nails, both of fingers and toes, is at times the site of obstinate abscesses and ulcerations. Shrewsbury[18] reported one case of cutaneous infection of the thigh, with recovery of an organism which resembled diphtheria morphologically and culturally, but did not produce toxin.

Areas adjacent to diphtheritic infections may also be involved, as the upper lip in nasal diphtheria with a marked resemblance to impetigo contagiosa. The external auditory canal, the retroauricular region, and the folds in the neck are not uncommonly affected.

Wound diphtheria also belongs in this group, and was a common finding in war-time hospitals. Postoperative incisions and tracheotomy wounds have also been found infected with diphtheria bacilli. Conjunctival diphtheria has been noted, and in one case was the primary source of a cutaneous diphtheritic infection.[19]

Diphtheria of the umbilicus is classed as an entity and is a usual location in infants with umbilical infections. Marked redness is present with little or no membrane. Montgomery[20] recently reported myocarditis and postdiphtheritic paralysis of the diaphragm following umbilical diphtheria.

COMMENT

According to the literature vulvovaginal diphtheria in children is still rare, but should be considered as serious an involvement as the faucial or pharyngeal forms. Toxin absorption seems to be slower from the vagina. Whether the early use of diphtheria antitoxin is the factor which prevents transmission of the pharyngeal infection to the genitalia, it is difficult to state. Local treatment does not seem to hasten negative cultures, and it is debatable whether it is of any benefit. General hygienic cleansing is allowed, using boric acid or any other mild antiseptic solution.

SUMMARY

A case of secondary vulvovaginal diphtheria with extension of the membrane across the perineum to the anorectal region is reported. A moderately large dose of diphtheria antitoxin was given, twenty thousand units intramuscularly and ten thousand units intravenously. Positive cultures for diphtheria were obtained from the nose, throat, vulva, vagina, and anorectal regions. Rapid healing of all the lesions, with no complications, followed serum therapy.

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PURULENT PAROTITIS IN THE NEWBORN

Case Report and Review of Literature

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PATHOLOGIC disturbances of the salivary glands in the newborn do not appear to be of common occurrence. The disorders of these glands usually fall under the headings of congenital anomalies, epidemic parotitis, or acute purulent infections. The latter have been reported in the literature under such varying titles as: "Acute Purulent Sialadenitis," "Acute Suppurative Sialo-adenitis," "Sialo-adenitis Neonatorum."

A recent typical case of this comparatively uncommon condition stimulated interest in us to review the literature on this subject.

CASE REPORT

Baby McK. was seen when fourteen days old. On the previous day her right parotid gland had begun to swell and her facies revealed the outline usually associated with mumps. Her temperature was averaging about 102° F. She was not unduly toxic. The physical examination revealed a female child weighing seven pounds ten ounces, normal, except for parotid swelling and the important fact that on inspection of the mouth we were able to express pus from Stenson's duct. The swelling responded to hot boric dressings, her temperature subsided in about forty-eight hours, and in the course of several days the infected parotid gland returned to normal. The leucocyte count was 13,600. The bacterial study of the pus revealed *Staphylococcus aureus*. She was fed on a lactic acid formula and her progress since then has been entirely normal (she is, at the present writing, about three and one-half years old).

The patient was a full-term child, being delivered by cesarean section, and had been breast fed until several days before her illness. The mother had no evidence of mastitis.

REVIEW OF LITERATURE

Dietrich[1] and von Reuss[2] state that purulent inflammation of the salivary glands is relatively rare, but that if it does occur, it is seen usually in early infancy. Plewka,[3] who has made the most recent and the most exhaustive review of the literature to date, states that in recent years sialadenitis is being reported with greater frequency; that although it is a definite clinical entity in the pathology of the newborn, it also may occur in nurslings and in children a little older. He was able, in 1921, to collect 52 published instances of sialadenitis. His feeling that cases are being reported with greater frequency is not borne out by our findings, because since his compilations, we were able to find only two further case reports by Decker[4] and Brandt.[5] Our case appears to be the third report of its kind during the last ten years.

Etiology.—The parotid was the salivary organ involved in 43 (81 per cent) of Plewka's 52 cases. The remaining 9 cases were acute purulent infections of the sublingual and the submaxillary glands. Bretschneider,[6] Durante,[7] Handrick,[8] Heath,[9] Hofstätter,[10] Lewin,[11] Nobecourt and Voison,[12] noted the staphylococcus as

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the etiologic organism. Hofstätter[10] and Perot[13] noted streptococci. Bannelier[14] Baum,[15] and Hofstätter[10] observed both staphylococci and streptococci; Ylppo,[16] *Bacilli coli;* Brindeau[17] and Guidi,[18] *Oidium albicans;* Bonnaire,[19] Kien,[20] and Plewka[3] demonstrated diplococci and staphylococci.

The pathogenesis of the malady is debatable and permits two explanations: (1) it may occur as an ascending infection from the mouth, or (2) by metastasis in a blood stream infection. Auerbach[21] and Ylppo[16] particularly favor the latter view, while Bannelier,[14] Bretschneider,[6] Heath,[9] Hofstätter,[10] Ibrahim,[22] Pallesin,[23] Perot,[13] and Thomassian[24] believe that the infection originates in the mouth and is spread by way of the lymphatics to the salivary glands.

Berndt, Buck, and Buxton[25] under the direction of Custer[26] at the University of Pennsylvania recently studied the pathogenesis of acute suppurative parotitis in dogs, confirming the experimental work of Rost [27] reported in 1914. They concluded that acute suppurative parotitis can be produced by the injection of bacteria into Stenson's duct, or by the injection of bacteria into the nutrient artery of the parotid gland; that infection of the gland is produced with much greater facility through the duct; and that the histopathologic picture in the two instances differs as follows:

Ductogenous Parotitis	*Hematogenous Parotitis*
1. Distention of ducts with purulent exudate.	1. Purulent exudate in ducts less marked. Ducts not distended.
2. Large ducts involved most extensively, small radicals least.	2. Large ducts relatively unchanged. Small radicals chiefly involved.
3. Extensive destruction of duct epithelium.	3. Epithelial lining of ducts intact or occasionally hyperplastic.
4. Periductal reaction most prominent where duct wall is broken.	4. Periductal reaction more uniform in distribution.
5. Periductal cell reaction chiefly neutrophilic.	5. Periductal cell reaction chiefly mononuclear.
6. No changes in blood vessels.	6. Swelling and hyperplasia of arteriolar endothelium with occasional beginning annular thrombus formation.

Plewka[3] believes that by the histologic analysis of his cases, he has demonstrated that an ascending infection of the salivary glands takes place in the newborn infant, and desires to express the opinion that the majority of cases occur after this fashion.

Bretschneider[6] states that the disease attacks premature infants relatively frequently (about 40 per cent). The coexistence of puerperal disease and fissures of the nipples may increase the possibility of infection. Stomatitis need not always be present. Brandt[5] observed an acute suppurative parotitis in a seven-day-old child with gonorrheal inflammation of the umbilicus.

These infections in infants have been attributed to deficient function of the not yet fully developed salivary glands (Bretschneider[6]) and to the acid or neutral reaction of the saliva (Mikulicz and Kummel[28]).

Clinical Course.—According to von Reuss[2] the first striking symptom is the swelling. It is situated according to the gland either over the cheek, in front of the ear, at the angle of the jaw or below the horizontal ramus of the lower jaw. The skin at first is generally unchanged; fluctuation at the beginning of the disease cannot usually be found. However, in the early stages, pus will ooze out of the excretory ducts by pressing on the swollen parts, that is, on the buccal mucous membrane above the alveolar margin of the upper jaw where the latter bends backward, and at the plica sublingualis or the frenulum linguae. The mouth of the excretory ducts may be reddened or somewhat dilated. The temperature is variable. The disease sometimes pursues its course with very high fever; in other instances this

may be slight or exist merely during the first few days. An afebrile course may also occur, particularly in debilitated children. The other general symptoms and signs vary in isolated cases. A certain tenderness of the glands affected is always present.

Prognosis.—Grulee and Bonar[29] state that the outcome depends upon the individual resistance of the child. In premature infants the outcome is frequently a fatal sepsis. In healthy full-term infants the prognosis is better. When extension to other glands and stomatitis occurs, the outcome is less favorable. Complications mentioned include penetration into the external auditory canal; burrowing of pus along the cervical vessels into the mediastinum and facial paralysis have been reported. Serious intestinal infections from swallowing of pus containing bacteria have not been reported.

Management.—Treatment at the beginning of the disease should be confined to rubiefacients. It has been recommended that the purulent secretion should be removed by regular pressure of the gland and the mouth; in particular the region of the duct should be carefully wiped out with antiseptic solutions (boric acid solution of hydrogen peroxide). Some advise early and even numerous incisions at various parts of the infected region, also at the point where the tense fascia parotideomasseterica interferes with the sensation of fluctuation (Baum[15]).

As with every disease occurring during the neonatal period, the nourishment must be maintained, preferably with breast milk. In many cases suckling was continued in spite of the disease, without any infection being transmitted to the maternal breast. However, Lequeux[30] noted galactophoritis at the same time. It would appear, therefore, to be advisable not to put the child directly to the breast but either to permit it to suck through a nipple-shield or to pump the breasts.

DISCUSSION

There can be little doubt as to the correct diagnosis. The discovery of pus exuding from the parotid duct permits no other explanation. However, this case brought up the interesting question: Does mumps occur in the newborn infant? The great majority of persons contract epidemic parotitis between the ages of five and fifteen years (Ker[31]). Nonpurulent contagious inflammation of the salivary glands occurs occasionally in the newborn (von Reuss,[2] Grulee and Bonar[29]). White,[32] according to the latter, described a case of mumps in a six-day-old baby during an epidemic of the malady. Gautier[33] noted swelling of the submaxillary gland in a newborn infant, twelve days after the mother had developed epidemic parotitis. Homans[34] described a unilateral swelling of the parotid gland in a newborn infant whose mother had mumps several days previous to her confinement, and Demme[35] reported a case occurring in the third week of life (Dietrich[1]). As a rule, mumps belongs to those diseases to which the newborn infant seems not to be susceptible (von Reuss[2]). Ker[31] and Shaw[36] in their respective monographs on infectious diseases make no mention of epidemic parotitis occurring at this tender age.

Another condition, possibly to be mistaken for the one described, is Kien's[20] congenital enlargement of the parotid. However, this occurs as a large, regular, turgid swelling of the parotid gland without any inflammatory symptoms. In the course of the first few weeks of life it gradually diminishes in size.

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310 MEDICAL ARTS BUILDING.

JACOB HEINE AND HIS CONTRIBUTION TO POLIOMYELITIS

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THE Heine family was a remarkable one in that it produced a series of justly renowned and resourceful orthopedic surgeons, the first of which was Johan Georg Heine (1770-1838). Four others, son, nephews, and great nephew were also celebrated. Jacob, one of the nephews (1800-1879), was born in Lauterbach, in the Schwarzwald, but for some reason or another did not begin his studies of ancient languages until he was twenty-one and then studied in a gymnasium in Würzburg. His uncle had a flourishing orthopedic hospital there and Jacob abandoned his idea of theology for medicine. He settled in Cannstadt and his orthopedic institution there was known throughout Europe. Jacob was honored with the title of Hofrath and Geheimhofrath and was ennobled by the Würtemberg crown.

In 1838, at the meeting of the medical section der Versammlung deutscher Naturforscher und Aerzte, at Freiburg, Jacob Heine reported a case of paraplegia which he had treated. In the official report in the *Bericht* published the following year on page 83 there is the following note: "Dr. Heine, of Cannstadt, spoke on paralysis which may follow convulsions and be accompanied with more or less deformity of the lower extremities. He showed that while these cases were formerly regarded as incurable, they may be markedly improved by using suitable machines and remedies. As proof of this he exhibited a twelve-year-old girl, who by the use of the above named means has been so far restored that she can use her lower extremities to some extent."

Heine wrote several articles and books, the most important of which was his *Beobachtungen über Lähmungszustände der unteren Extremitäten und deren Behandlung,* which was published in 1840, in Stuttgart, by Franz Heinrich Köhler. In 1860 a second edition appeared under the title of *Spinale Kinderlähmung.* From the first edition the clinical description of the disease may be quoted:

> When we bring together the principal symptoms of the recorded cases, their onset, course, and termination, we find, in general, the following clinical picture.
>
> Healthy children of normal birth, for the most part who appear in blooming health, from the age of 6 to 36 months, exceptionally older, who have previously enjoyed perfect health are affected either with or without the following evidences of being unwell: turning the eyes, etc., suddenly with the appearance of heat, congestive or irritative conditions, fever, throat irritability, crying, sleepiness without real sleep, and when there is teething with the added appearances of *dentitio difficilis,*

also sometimes with the symptoms of a disturbed course of an acute exanthematous disease. In this case soon light or severe convulsions occur which are repeated at shorter or longer intervals.

In other cases the disease comes on without the above symptoms with sudden convulsions or nausea, falling of the body, foam at the mouth and nose, cyanosis, etc.

Sometimes all these manifestations are wanting or are present only in a very slight degree and the paralysis comes, so to say, unmarked.

Now after the disease, as described, has run its course, sometimes shorter, sometimes longer, severely or mildly, with or without convulsions, there is a lessening of the symptoms—(*Paralysis suspendit convulsiones*)—so that the affected child is in the greatest danger of life and lies quiet, pale, and weakened, opens the eyes and looks about as if it had awakened from a deep sleep.

BEOBACHTUNGEN

über

Lähmungszustände der untern Extremitäten und deren Behandlung.

Von

J. Heine.

Mit 7 Steindrucktafeln.

Stuttgart.

Fig. 1.—Title page of Heine's book published in 1840 in Stuttgart.

No sooner do the troubled parents rejoice in the glad hope of the recovery of their loved one than they, with fright, discover that the lower extremities are paralyzed. There is often, too, a paralytic weakness of one or both arms and of the thorax itself so that the child can no longer sit erect. This complication is, however, mostly only temporary in that the power of movement in these parts again is soon restored.

Interesting is the observation that under the same manifestations and by originally simultaneous paralysis of lower and upper extremities often only one of the former or single muscles of one or both feet become permanently paralyzed.

In the meantime the questionable paralysis is not complete, that is, there is no permanent loss of sensation together with every trace of spontaneous movement of the affected extremities; on the contrary the sensation is not disturbed and movement is retained to a certain degree as the children feel every touch as well on the paralyzed side as on the sound one and are able more or less to draw the lower extremities up and down, although as a rule they cannot as easily draw them to them as they can extend them, and perform adduction, abduction, and rotation.

Especially to be noted is the constant fact that the paralysis is always worst at the beginning and then after a time goes back to a lesser degree. So also, as the muscles which go from the pelvis to the hip they retain the most life and the further down the muscles are the less the power so that the foot only can be moved spontaneously a very little.

The temperature of the affected parts sinks soon after the primary attack and the longer the duration of the paralysis the lower the temperature, especially from the knee downward so that a Reaumur thermometer set upon it sometimes falls to 14°. The upper extremities are always a little warmer. From the lessening of the *turgor vitalis* there is even in the first days after the paralysis flaccidity and atrophy. Standing and walking in the paralytic form is completely done away with, as the children sink down on trying to stand them on their legs. In the hemiplegic and

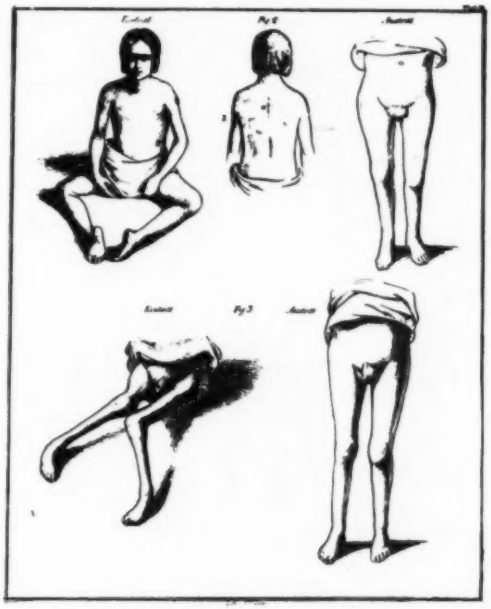

Fig. 2.—Some of Heine's cases before and after treatment, 1840.

lighter cases it is possible by support and help in some to do a little. Only exceptionally is there a permanent weakness in the function of the bladder and rectum.

With the increase of years the growth of the paralyzed extremities progresses regularly but the limbs become thinner and are deformed later, according as to whether the children crawl on the floor and bring their extremities in bent positions peculiar to their paralysis in an often horrible way, so that it is not rare to see all the known varieties of deformity of the limbs in one and the same individual. In a paraplegia the limb that is paralyzed the most shows less growth. In hemiplegia and the other paralytic affections single muscles are in a similar condition through which frequently a sinking of the pelvis takes place.

In cases of prolonged duration the spinal column leans to one or other side without producing pain.

Only occasionally does one or both arms remain thinner and weaker.

Moreover, the most of the patients later in spite of the paraplegia and continual sitting enjoy relatively good general health and have good digestion and regular bowel movements.

In regard to the mental and sense functions it must be added these are in no way disturbed. The most of the patients are quiet and gentle disposition and some even talented.

In his account of the pathology Heine refers to the first autopsy recorded which is that made by Hutin (Nasse's Sammlung zur Kenntniss der Gehirn und Ruckenmarkskrankheiten, 2 Heft S. 10, 1825, quoted by Heine, P. 54). This was on a man, forty-nine years old, whose atrophy and deformities were stated as being indescribable. His

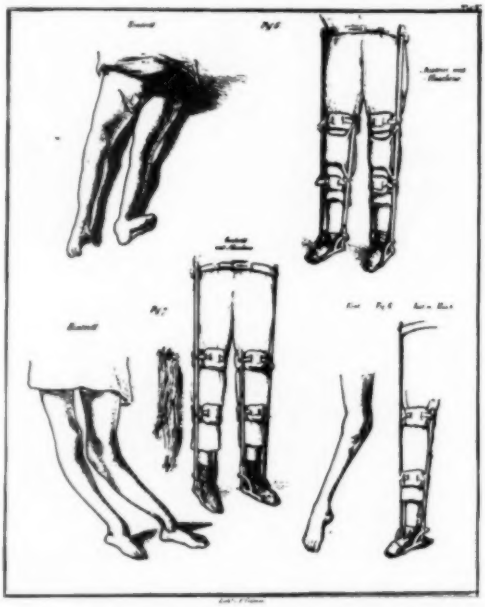

Fig. 3.—Some of Heine's cases with apparatus devised by him, 1840.

trouble dated from seven years of age. The central nervous system was normal to the eighth dorsal nerve but below that the cord was atrophied and where the lumbar enlargement should be it was reduced to the size of a goose quill (Feder) and was hard and it was not possible to make out the gray matter. The nerves were thin, yellow, dry, and hard. The blood vessels in the affected parts were very small and the muscles themselves were like whitish bands.

Heine called attention to the general atrophy of the affected parts involving length and circumference of the bones, the muscles, the arteries, veins, and lymphatics, the tendons and coverings of the joints. He also noted the deformities of the spinal column. He placed the

lesion in the anterior part of the cord and thought it due to a congestion followed by a serous exudate.

He sharply differentiated the disease from the spastic paralysis of early life and cited several cases to show the clinical differences, particularly the onset and course, the involvement of the mental faculties, the headache, dizziness, shimmering before the eyes, tinnitus aurium, and sometimes pain on the paralyzed side, the absence of atrophy or only slight wasting, the involvement of bladder and rectum, the rapid onset of paralysis, the spasticity of muscles and joints, and the absence of a tendency to deformities of the spinal column.

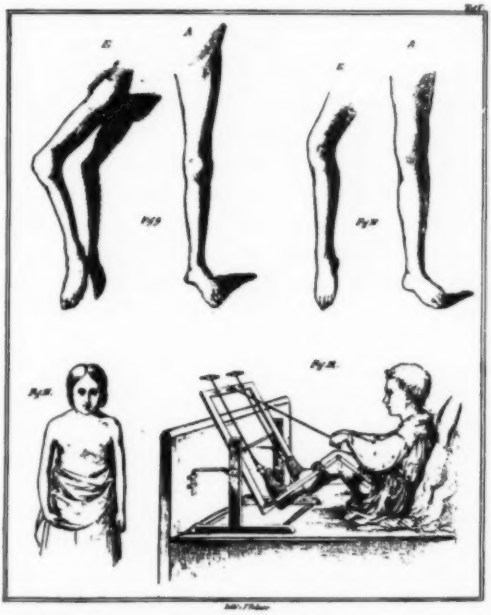

Fig. 4.—Correction of deformities and apparatus for exercise. Heine, 1840.

As to prognosis he noted the favorable outlook as to life in contrast to the spastic cases so prone to bed sores, edema and fevers followed by death. He noted, too, the improvement to be obtained by othopedic treatment after other methods had failed and pointed out that the hope of improvement depended on the following considerations:

1. The prognosis is better the less the atrophy and the greater the amount of movement present, particularly in the thigh.

2. The younger the patient the less is the deformity and hence the prognosis is better [It must be borne in mind he was dealing with late cases]. In the young the atrophy has not progressed to such an extent and in these cases the muscles can be better developed.

3. The length of the cure and the care used in it he also regarded as important. The cure must not be regarded as finished when the deformities were straightened out and the child able to move with braces but continued with unabated diligence for a number of years.

Heine's idea of therapy as set forth in his first edition consisted:

1. In trying to stimulate the affected nerves and part of the cord with a view to causing a resorption of the exudate in the cord.

2. To correct the deformities and to use such mechanical devices that would enable the patient to stand and walk and to permit the patient to move the paralyzed extremities when sitting and lying.

3. To improve the general condition.

For the first indication he tried strychnine or extract of nux vomica, rhus toxicodendron and phosphorus, the latter applied externally in solution by rubbing it on. He did not note any change except increase in temperature and sweating of the affected parts from strychnine and increased movement in one patient. The rhus was ineffectual, but he thought the phosphorus improved the general condition.

For the second indication he used tub, steam, and steam-douche baths, changing from one to the other and after the warmth, rubbing with salve with attempts to correct the deformities. He used apparatus to get rid of the contractures, gradually increasing the tension. When these were relieved, the foot deformities were next given attention, using apparatus and tenotomy. He also devised a machine to exercise the muscles, an adumbration of the Zander apparatus. With this he was able to give measured exercises. In addition, mud baths, in which water from chalybeate springs was mixed, were given, both locally and generally.

In 1860, as noted above, Heine, who by this time had been ennobled to von Heine and had been the recipient of numerous honors, rewrote his monograph and the J. G. Cotta'scher Verlag, in Stuttgart, published it, with the title of *Spinale Kinderlähmung*. From 78 pages and 7 plates it was increased to 204 pages and 14 plates. He included a table of 47 cases which he had treated, and he states that he had had more than 150 cases under his care. To his outline of his cases he added a review of the literature as regards the etiology and states "Another author Colmann (Colmer?) describes an epidemic outbreak of the same." Whether this is to be taken to mean that Heine grasped the idea that the outbreak was of an infectious disease is, of course, questionable, but it is perhaps the earliest use of the word epidemic in connection with the disease.

His chapter on differential diagnosis is extremely good and he details by way of contrast 10 cases of "hemiplegia cerebralis spastica," 8 cases of "paraplegia cerebralis spastica," and considers progressive muscular atrophy.

In the treatment he made a great step forward in recommending not only the treatment of the deformities but their prevention by the use of rubber bandages, as suggested by Duchenne, or wire and leather apparatus.

Heine was the first to make an extended report on poliomyelitis and his monograph is a milestone in the history of the disease.

COMMON SENSE IN INFANT FEEDING

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THE subject of infant feeding which formerly occupied a position of great prominence on the programs of pediatric section meetings is seldom discussed nowadays, for according to most authorities, its problems have been solved. At present the routine practice is simply to give a formula with sufficient calories in a more or less concentrated form, containing ample carbohydrate and an appropriate amount of orange juice and cod liver oil. The caloric requirement is determined by using an energy quotient, the number of calories per pound of body weight varying according to the age and size of the baby. Provided the baby gets the required number of calories it matters little what formula is used; some prefer sweet, some sour milk mixtures. For the convenience of the physician, various commercial firms manufacturing infant food materials distribute tables (to the physician only) which give the number of ounces of a mixture to be given at a feeding to a baby of any age and weight. Let me illustrate with an example taken at random: a baby aged two months, weighing eleven pounds. According to the table of a manufacturer of evaporated milk, this baby should receive a certain formula and be given five feedings of four and one-half ounces. A firm making a carbohydrate to be added to cow's milk recommends for the same baby seven feedings of four and one-half ounces; another six feedings of five ounces. In this light, then, the feeding of an infant ceases to be a problem. One merely makes up a mixture as directed, administers so many ounces every three or four hours and the baby is expected to thrive.

This method of "table" feeding is advocated also by most of the leading textbooks of pediatrics; it is employed in the teaching of students and internes. The arrangement of the ingredients may differ in the recommendations of various authors, but all advocate the use of a specified amount of a formula for a baby of given age and weight.

From observations made in private practice it has become my firm conviction that the above mentioned stereotyped methods are unphysiologic, unsound, and are responsible for two of the most upsetting symptoms among infants artificially fed, namely, crying and anorexia.

If we take an example from that archaic method of infant feeding, namely, breast feeding, we learn that babies on the breast show a surprising variability in the amount of food they take at different feed-

Chairman's address at Section on Pediatrics, California Medical Association, Del Monte, April 27, 1933.

ings during the same day, and by different infants of approximately the same age and weight. Thus, of three breast-fed infants two months of age weighing approximately eleven pounds, one may average four ounces at a feeding, with variations of from two to six ounces; another may average five and one-half ounces with variations from three to six and one-half ounces; and a third may average seven ounces with variations from four to nine ounces. On the bottle and according to rule these same infants each and all would require four and one-half or five ounces to a feeding. Treated in that way, what would happen? At some feedings baby number one would refuse one or two ounces; baby number two would occasionally refuse an ounce or more, but at other feedings it would be dissatisfied and cry; while baby number three would be habitually unsatisfied and probably would cry after four of the five feedings. The mother of the first baby would be urged by her physician to force her baby to take more than he wants. As a result of this forced feeding, irritability and fussiness would become the initial symptom of a first-class "feeding problem" or "behavior problem" and would lead eventually to anorexia, that prevalent modern condition for which we are justly blamed. The mother of the third baby would be advised to "let him cry it out" "not to spoil him," "to get the gas up and give water." Even so, she would have a dissatisfied, unhappy baby.

A "well baby service" in private practice offers the opportunity for observing the behavior and reactions of babies which is not afforded by a hospital service. A mother is more sensitive to the crying of her baby than is the ward nurse to her patient. The mother's whole time is devoted to the observation of a single baby; its crying affects her acutely and she reports it to her medical adviser promptly. The hospital nurse, occupied with the routine care of several babies, some of them sick, is not disturbed when a baby cries after feeding. She knows it will stop eventually, and she expects babies to cry anyway.

My observations of babies has been that the two chief causes of crying, if we exclude gas or air, are, first, the forced feeding of a specified quantity of food which is more than the baby wants at that particular feeding, and second, habitual underfeeding. The first group cry because they are irritated by forced feeding, the second because they are hungry. The explanation for both situations lies in the rule of thumb method of giving a certain number of ounces at a feeding and this justifies criticism of our present type of pediatric supervision.

It must be admitted that one of the great virtues of the supervision of the infant by the pediatrician or the general practitioner lies in the establishment of proper habits on the part of the infant. As a baby can be trained to eat at convenient intervals of three or four hours instead of eating when hungry, so in the majority of instances it can be trained to eat a specified amount at a feeding and be satisfied

until the next feeding. The average mother, I agree, needs a definite written feeding schedule, and should not depart from this set program without consulting her doctor. I firmly believe that under proper guidance the mother is relieved of the greater part of the natural anxiety that is common to all mothers, and that a well baby service properly managed is a sound arrangement for both the baby and the mother. The point I wish to make is that babies are individually different, requiring individual feeding, and that no rule of thumb or tabular scheme may be adapted to all babies, especially with regard to the quantity of food.

The practice which I have adopted and recommend is as follows: first select a formula which is sufficiently concentrated, that is, affords approximately twenty calories to the ounce. Second, begin with the conventional number of ounces at a feeding in accord with the age and weight of the baby. In a few days the mother or nurse will learn whether this amount is excessive or inadequate. If excessive the quantity at a given feeding may be reduced and when necessary the caloric value strengthened (concentrated). If inadequate, the amount should be increased until a point is reached where the baby is satisfied, even though this amount may seem high in comparison with published tables. With the aid of weekly, or if necessary daily, reports the amount may be readjusted to the individual case. An adequate weekly gain may be secured by arranging the strength of the formula, and likewise the character of the stools may be controlled.

It is now generally accepted that the size of infants and their growth follow hereditary laws. Some babies are small and gain weight slowly. These usually require a small amount of food. Others are larger, grow faster, and require a greater quantity of food. The activity of the infant will also influence the amount of food necessary. Ordinarily the appetite affords the best indication of the food requirement and it is not easy to overfeed a baby, provided the formula is correct. A vigorous active boy of large parents may consume twice as much food as a quiet girl baby of small parents. My plea is for the use of good judgment, permitting the appetite to guide the feeding of the artificially fed infant as it guides the infant at the breast.

CHOREA IN THE NEGRO RACE

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A SURVEY of the literature leads one to believe that chorea in the negro is rarely seen. The inquiry instituted by Dr. S. Weir Mitchell many years ago to southern physicians indicated that the occurrence was rare. In reply to this Sinkler[1] reported a case of a nineteen-year-old negress whose mother was a mulatto. He adds, "Several doctors of Virginia wrote to Weir Mitchell that they considered the disease as common in one race as the other," and that Dr. S. H. Stout of Chattanooga had figures to show it more prevalent in the negro race. Others[2, 3] reported cases. Although Polk had charge of the medical affairs of six colored regiments in the Civil War and was in command of a large colored area during the reconstruction period, he never saw a case of chorea in a full-blooded negro; however, Skinner[4] found a case in an eighteen-year-old girl. The records of the Philadelphia Infirmary were reviewed by Osler[5] who found the disease in five mulattoes but failed to find a single full-blooded negro choreic. The proportion of colored to whites was as one to twenty-five, and there were many cases of chorea in the whites, hence he concluded the disease rare in the negro. A very interesting report is that of Roy[6] in 1892, who cited seven cases of chorea in the negro race. At that time he suggested this should no longer be considered a rare clinical entity, for only ten years prior hysteria was believed nonexistent in the colored race. Despite these reports, the findings of Weir Mitchell and Osler seemed to dominate medical opinion.

Most modern textbooks of medicine[7, 8, 9, 10] and neurology[11] mention the disease as rare in the colored race. All are not in accord with this statement. In his monograph on rheumatic heart disease, Coombs[12] takes a different stand. While he has found no report of cases in native Africans, he admits the possibility of chorea in the North American negro; yet there are no figures to show its incidence. Kreschner[13] writing in Tice *Practice of Medicine*, credits Sacks with having seen a number of negro children with chorea in the New York Polyclinic. Reviews of fairly large series of cases by Abt,[14] Helmholtz and others[15, 16, 17, 18] fail to mention negroes, nor is the disease noted in this race in the excellent papers of Gerstley[19] or Epstein.[20] The painstaking review and analysis of chorea gravidarum by Wilson and Preece disclosed only one negress in 800 patients. This case, though quite typical, suffered a mild attack.

From the Cardiac Follow-up Clinic, Cook County Hospital and the Department of Medicine, Northwestern University Medical School.

The divergent opinions of different authors, the scanty reports of cases and the lack of a review of this subject led to a careful inspection of the records of children in the Cardiac Follow-up Clinic at the Cook County Hospital. The Children's Division is composed entirely of children under fourteen years of age who had previously been admitted to Cook County Hospital. Most of them were admitted to the pediatric service as: Acute rheumatic fever, chorea, nephritis, endocarditis, etc. The remainder entered other services as: scarlet fever, diphtheria, tonsillectomy patients, etc., and in them the diagnosis of a complicating heart lesion or chorea was noted. Through the efficient activities of the social service department, all cases with cardiac notation were directed to the Follow-up Clinic. Patients in the clinic are ambulatory and are given necessary care and advice. When this is insufficient, or the rest at home inadequate, or decompensation impending, these patients are referred to convalescent homes or readmitted to the Cook County Hospital. Thus, a review of cases in this group represents a fair incidence of cardiac disease in a selected "cardiac group," and it is of limited value in regard to comparison with the general population.

METHOD

Case records of children regularly attending the clinic were studied. A fine rapid tremor of the protruded tongue, purposeless quick movements of the fingers and hands, facial grimaces, together with a slight pyrexia, were essential in the diagnosis of acute Sydenham chorea. When the diagnosis of previous or subsequent attacks was relied on by the history alone, a four to six weeks' course with irritability and restlessness was sought. Most of the cases were observed in the clinic during the past three years, within which time recurrences assured the diagnosis of chorea.

RESULTS

A series of 165 cardiac patients was selected, of which 58, or 35 per cent, were choreic.

	WHITE		NEGRO		
	MALE	FEMALE	MALE	FEMALE	TOTAL
Rheumatic fever	31	31	8	13	83
Chorea	22	27	4	5	58
Miscellaneous	8	12	1	3	24
Total	61	70	13	21	165

The age of these groups was approximately the same in all. In both the white male choreic and the white female choreic, ages ranged from 6 to 13 years with an average age of 8.2 years. Of the four col-

ored boys the ages were 4, 7, 9 and 12 years; while the five colored girls' ages were 7, 7, 8, 9 and 13 years.

Associated pathologic conditions in the white group were variable and included slight cardiac hypertrophy, polyarticular enlargements, repeated tonsillitis and chronic valvulitis. In the female colored group two had mitral heart disease, one of which had a fairly high grade stenosis. The remaining three showed no evidence of endocardial or myocardial damage. There had been two attacks of chorea in each of the first two, while a single occurrence was seen in the latter ones. Two of the negro boys were without any apparent cardiac injury while the other two were affected. One had a moderate mitral heart lesion while the other was severely damaged. He had suffered three attacks of chorea and now has a high grade mitral disease, aortic insufficiency and an adhesive pericarditis. It is to be mentioned that none of these cases (colored group) has been decompensated. No comparison with the white choreic group is attempted because of the small number of negro choreics reported.

DISCUSSION

Formerly it was believed that chorea and acute rheumatic fever were independent diseases. Following the painstaking histologic studies of Coombs,[12] there is an ever growing expression that they, like the polyarticular swellings and the subcutaneous nodules, are part of rheumatic fever. The pathologic studies of Greenfield and Wolfsohn,[22] Castren[23] and Swift,[24] show a similar lesion in chorea and rheumatism. The only differences that occur can be explained by the different supporting structures. In the one case it is the brain, the other the heart, or subcutaneous tissue. It has been long accepted that acute rheumatic fever occurs in the colored race. To explain the absence of chorea in the negro one would be forced to postulate a new and different immunologic reaction. However, the occurrence of chorea in the negro obviates this explanation.

Cases of chorea in the negro race have been published sporadically from 1872 to 1900. After that time apparently no further cases have been mentioned directly, and a majority of texts state that it rarely is seen in the negro. While it is admitted that our clinic is composed of a "select cardiac" group, yet the incidence of chorea is about the same in both races. One hundred and thirty-one white children comprised the clinic, or 79.39 per cent of the total number. The negroes number thirty-four, or 20.61 per cent of the clinic. Chorea was found to affect 37.77 per cent of the white children and 26.73 per cent of the colored children. It is possible that the alleged rarity of chorea is merely a carry-over from the older texts and that it, like the absence of hysteria in the negro race, is in need of more accurate study.

CONCLUSIONS

1. Acute Sydenham chorea is seen in young negroes.

2. It apparently has the same characteristics in both the white and the colored races.

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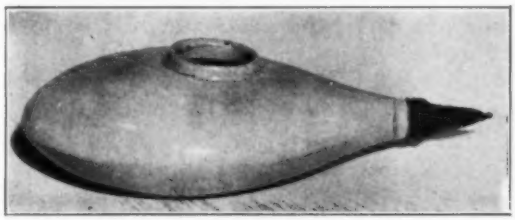
636 CHURCH STREET

ANTIQUES OF PEDIATRIC INTEREST

T. G. H. Drake, M.B., F.R.C.P.(C).

EARLY feeding bottles complete with the original nipple are of great rarity. In the author's collection of thirty-five pottery feeding bottles the specimen illustrated is the only one so equipped. The nipple, 3 cm. in length, is composed of thin chamois coarsely stitched along both sides to give it a fingerlike shape. No insertion of sponge is found in this particular nipple.

The nipple has been composed of many materials. In a pamphlet "Regime pour les pauvres," circa 1720, the knob of the pewter feeding bottle is described as being "covered with a piece of fine cloth or with a bit of chamois attached and sewed with thick thread. This appendage is of the size and form of the human nipple. The knob of the flask should not be covered with more than three or four thicknesses of cloth, and these ought to be washed from time to time to ensure that they do not contract a sour taste."



Feeding bottle with original chamois nipple. Circa 1830.

George Armstrong, 1771, fastened to the end of his cow's horn feeding bottle "two small bits of parchment shaped like the finger of a glove, and sewed together in such a way that the food poured into the horn can be sucked through between the stitches."

Von Rosenstein, 1776, recommended fastening to the horn "a tanned skin of a cow's teat, or if that is not to be procured, we may use any other thin skin pierced with many small holes."

De Miollis, 1780, recommended a nipple of wood enveloped in fine cloth.

In Baldini's feeding bottle, 1786, the crystal bottle ended in a lobe-shaped mouthpiece of gilded metal. This was filled with a piece of fine sponge, the projecting tip of which was presented to the infant. One was cautioned to wash the feeding bottle and sponge several times a day with lukewarm water.

Strune, 1802, also used the sponge: "On the orifice of this inhaler (feeder) may be fixed a piece of sponge, cut in the form of a nipple,

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and covered with fine linen, but in such a manner that the child may not draw out and swallow the sponge itself. If a vessel proper for this purpose cannot be readily procured, a strong phial may be substituted, the mouth of which should be stopped with a cork previously perforated with a red-hot wire; next, a piece of sponge may be fastened to the top of the vessel in the manner before described."

Burns, 1811, wrote that "the cow's milk mixture is not to be given with the spoon, but the child is to suck it of a proper heat out of a teapot which is made for the purpose, and which has a piece of soft cloth tied over the perforated mouth."

"The teat of washed chamois leather which could be had at any druggist's ready for use" was the one recommended as late as 1842 by Evanson and Maunsell.

Churchill, second American edition, edited with additions by Keating, 1856, gives details regarding the nipple and its care: "The only care, beyond cleanliness, required concerns the nipple; it may be formed of chamois leather, in shape and size like the little finger of a glove with a perforation in the end, and it should be changed every time it is used; or a prepared calf's teat may be tried, and this, I think, is better, as it has more firmness, and does not collapse and close from the pressure of the infant's mouth, which the chamois leather is apt to do unless prevented by the inserting of a small piece of sponge. After each feeding the teat should be removed, rinsed, and put into spirits of wine and water until again wanted, and the bottle should be washed carefully with hot water. It is of consequence that the nipple (whether a teat or of leather) should be so long as to prevent the gums of the child coming in contact with the bottle neck; the infant, it must be remembered, does not suck with the front of its mouth, but with the back part. As a substitute for chamois leather or a calf's teat, M. Dardo, of Paris, has invented a nipple of thin electric cork, and someone else, whose name I do not know, one of ivory, from which the earthy matter has been removed, and which is flexible and elastic. I have tried them both, but have not found them so satisfactory as the calf's teat; they appear to me far too short."

The rubber nipple was used in 1878 by Duncan, who wrote: "The best feeding apparatus for the infant is a bottle holding about four ounces, with a black rubber nipple for a cap. This is the easiest kept clean. The chief objection to it is that it is hard to draw. A long tube passing through the cork with a valvular opening, having a glass tube to pass into the milk is the one that is usually chosen. This apparatus needs the most careful attention, or the milk becomes tainted—the sulphur in the rubber, like the sulphur in the casein, starting fermentation. If the milk stands in the bottle only fifteen minutes, it is unfit for use. On the whole it is safest to always recommend the black rubber-cap nipple. The white contains more sulphur, and some say also zinc."

Critical Review

NEUROLOGIC CONDITIONS IN INFANTS AND CHILDREN CRITICAL REVIEW

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NARCOLEPSY

IN VIEW of the increasing number of case reports in the literature and inasmuch as successful symptomatic treatment has been described by several writers, a brief review of this condition is of interest.

Narcolepsy, first described by Gélineau[1] in 1880, may be said to be characterized by two chief symptoms, i.e., an irresistible desire to sleep, and a feeling of generalized weakness following laughing or other emotional disturbance. The desire to sleep may occur at any time, regardless of the attending circumstances, and is unrelated to the amount of nocturnal rest; the patient may suddenly go to sleep while reading, eating, talking, walking, or working. This sleep resembles the "normal" sleep of an individual, although it may at times be accompanied by hallucinatory dreams which in themselves may cause the patient to awaken. As has been pointed out by Adie[2] there are occasions, however, when the weakness or cataplexy may result in closure of the eyes and inability to articulate, thereby giving the impression of sleep. The attacks of generalized weakness, or the cataplectic attacks, are precipitated by emotional disturbances, the most common of which is laughter. In fact, many of these patients refuse to laugh, knowing well that any such act will be immediately followed by a generalized sensation of weakness which may result in their collapse; less frequently fear, anger, or distress may produce this same sensation.

The etiology of this condition continues to be obscure, although there is good reason to believe that in certain cases it may be symptomatic, i.e., secondary to trauma, disturbances in glandular functions, infection, etc. Due to the fact that an increased number of these patients have been seen since 1918 (the year of the epidemics of influenza and encephalitis) it has been suggested that there might be a relationship between epidemic encephalitis and narcolepsy. Wilson,[3] however, in his excellent review of the subject in 1928 makes the following statement: "Were one to argue from these considerations, a case might be made out for an actual increase in disordered conditions of sleep somehow related to the times in which we are living, and their ascription to processes out of epidemic encephalitis might be plausibly offered as one explanation, but at present I am far indeed from being convinced of any frequent etiological association of the latter with the former." In regard to other etiological factors he states: "The data which have just been examined . . . . . are sufficient to show how diverse and heterogeneous is the etiology of

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the narcoleptic syndrome. To assort the casual factors is a matter of no little difficulty; a provisional arrangement might be made along the following lines:

"1. Traumatic group.
"2. Psychopathological group.
"3. Endocrine group.
"4. Epileptic group.
"5. Toxic-infective group (epidemic encephalitis, etc.).
"6. Circulatory group.
"7. Pressure group (cerebral tumors, etc.).
"8. Group in which no Grundkrankheit has been discovered."

Trasch,[4] Spiller,[5] Weech[6] and others have reported cases in which there appeared to be a definite relationship between endocrine dysfunction, encephalitis, and trauma and this disturbance.

The age incidence is such that narcolepsy is more frequently encountered in adults than in children. Cave[7] in a report of 42 cases found that the age of onset varied from nine to forty-six years with an average of twenty-five years in males and from eight to thirty-seven years, in females, with an average of nineteen years. Levine,[8] in a study of the published cases, found only 4 in which the age incidence was under ten years. In Cave's cases 34 were males and only 4 females; in Wilson's there were 37 males and 7 females, while in Adie's group of 20 (17 from the literature and 3 of his own) there were only 3 cases in females. Judging from the increased number of case reports of this condition in children during recent years one may later find that the disease is not as rare in this age group as the present statistics would lead us to believe.

The diagnosis can usually be established without difficulty if both symptoms are present. If the chief complaint is that of recurrent or frequent attacks of sleeping, there is reason for possible confusion before the proper diagnosis can be established. In some cases the cataplectic attacks may occur alone or for several months before the sleeping attacks appear, and it is in this group that one might be misled by considering epilepsy or petit mal. However, careful questioning will reveal the fact that the attacks of weakness occur only after *emotional* disturbances (especially laughing), are not accompanied by loss of consciousness (for these patients can be readily awakened), or by loss of sphincter control, and that they are not followed by stupor or prolonged periods of unnatural sleep.

The treatment of narcolepsy, like all idiopathic disturbances, has passed through many forms and processes and the result has always been the same. However, in 1931, Doyle and Daniels[9] reported successful symptomatic treatment by the oral administration of ephedrin sulphate. Quoting their summary: "Six patients suffering from narcolepsy were treated with ephedrin sulphate. Five were completely relieved of the essential symptoms of irresistible desire to sleep without apparent cause and cataplexy. The sixth patient is relieved of cataplexy and hypnagogic hallucinations, and somnolent tendencies are markedly improved." Similar results have subsequently been reported by Wahl,[10] Collins,[11] and Jacobsen.[12] The usual dose has been 3/8 of a grain, three times a day, although at times it has been necessary to increase this to 3/4 of a grain three times a day before satisfactory results could be obtained.

MICROCEPHALUS

During the past few years attention has been directed toward the various factors that might be concerned in the production of microcephalus, and its resulting idiocy. The condition per se is not very common, as probably not more than one out of every hundred mentally retarded persons belongs in this group.[13] However, the disorder is of such a serious nature that any procedure or procedures that might be conducive to its development should be carefully considered.

Aside from the familial tendency,[14, 15] there appear to be three possible etiological factors: (1) developmental defect, (2) trauma, and (3) injury to the brain tissue following x-ray or radium therapy. From the developmental standpoint, the condition represents an arrested development at about the fourth or fifth month of pregnancy, although it is not clearly understood what physiological factors influence these changes. That trauma to the brain must be related to the production of microcephalus there can be little doubt, for a history of intracranial hemorrhage either as the result of trauma at birth or secondary to hemorrhagic disease of the newly born is frequently obtained in these cases. As a result of this injury there apparently follows not only a diminished tendency for further growth but also actual atrophy which can be demonstrated by postmortem examination and by encephalography. This is one etiologic factor, i.e., trauma, that has not received sufficient investigation.

The one probable etiologic factor that has received a great deal of attention during the past few years has been the possible effect of radium or roentgen ray therapy upon the gravid uterus. Experimental evidence[16, 17] has shown that either of the above named procedures frequently results in defective embryos or offspring of animals. As a result of their observations on x-rayed mice, Little and Bagg[18] made the following statement, "The experiments here recorded justify, we believe, the recommendation of extreme caution in the use of radium or x-ray therapy on human individuals who are likely ever to serve as parents after they have been treated." In a later publication Bagg[19] further emphasized this statement by the following conclusion, "Irradiation of the unfertilized ova or the spermatozoa may result in either completely destroying the functional activity of these cells, or so modifying their structure that the resulting offspring may be defective." The same view was expressed in regard to radiating the fertilized ovum. Bailey,[20] Mendell,[21] Pemberton,[22] Ries,[23] Corscaden,[24] and others have pointed out the danger of producing defective children whenever radium or roentgen ray therapy is employed for the treatment of gynecologic conditions in pregnant women. The literature[25, 26, 27] contains many reported cases of microcephalus following these procedures. Hickey and Hall,[28] after analyzing the results of a questionnaire sent to radiologists, found that the replies could be divided into two groups, one in which *diagnostic exposures* were made, and another in which *radiation therapy* was employed. Diagnostic exposures were made in 76 cases with 69 full-term normal babies. The 7 cases that were not normal included miscarriages, induced labor on account of uremia, etc., but no cases of microcephalus. "It would therefore seem that the use of diagnostic exposures as predicated by this group is not attended with danger to the fetal structures." In the group receiving radiation

therapy, there were 13 cases, 10 of which went to full term with *normal children;* there was one premature infant, one stillbirth, and one case of incomplete abortion. Again, there were no cases of microcephalus.

In a review of two hundred pregnancies in women who had been subjected to pelvic irradiation published in 1929,[29] and in a previous paper published in 1928,[30] Murphy presents "the largest collection of reported cases available for study dealing with the possible relationship that may exist between the maternal pelvic irradiation and the health of subsequent children." From these cases, all of which have been carefully studied and analyzed, the following conclusions are drawn:

1. "It appears reasonable to suspect that certain of the gross structural defects found among children, irradiated *in utero*, result from such irradiation.

2. "There is as yet no definite indication that *ovarian irradiation, prior to fertilization*, has any detrimental influence upon the health or development of any subsequent children."

The diagnosis of microcephalus is not difficult, as the small head (usually seventeen inches or less), the narrow and receding forehead, flat occiput, pointed vertex, prominent nose, and long arms and hands are characteristic. Roentgenologic examination of the head shows a small skull with a large jaw which is out of proportion to the former. Encephalographic studies frequently reveal only a small amount of air in the subarachnoid spaces but large and symmetrically dilated lateral ventricles.

Postmortem examination of the brains of these patients shows the following: "In removing a microcephalic brain one usually finds a noticeable loss of that normal convexity of the hemispheres. A hypoplasia involving practically the entire cortex yet more obvious in the parietal and occipital lobes is usually noticeable. Rarely is there a numerical loss of convolutions, though they may vary profoundly in size and shape. Occasionally an absence of sulci is noted. Internal hydrocephalus, porencephaly, pseudoporencephaly and atrophic sclerosis of the hemispheres are reported to have been found not infrequently.[31]"

Treatment of this disorder is ineffective. In view of the fact that the anterior fontanel closes prematurely, various surgical procedures have been attempted to prevent this premature closure of the skull, but none of them have proved of value. Glandular therapy is mentioned only to be condemned. Institutional care is advisable when the management of these children at home becomes impossible.

MONGOLISM

The etiology of mongolism, or as it is more commonly and incorrectly called, Mongolian idiocy, continues to be a little understood condition. Alcoholism, syphilis, endocrine disturbances, inheritance, and age of the parents have all at one time or another been considered and later discarded. Down[32] suggested that the physical likeness of these individuals to the Mongolian race might be due to an admixture of Mongolian blood among the Europeans. Crookshank[33] supported this idea and brought forth many resemblances which he believed common to racial Mongols and this type of imbecility. However, it has been well established that such a theory is not tenable. Penrose,[34]

after a study of the four blood groups in 166 Mongolian imbeciles, concluded that "the results do not support the hypothesis that this class of imbeciles has any relationship to the Mongolian race." Another observation tending to disprove this theory is that of Brousseau[35] who in 1928, listed the occurrence of mongolism in non-Mongolian families as occurring in twenty-eight different countries; since that time other countries have been added.

The occurrence of this form of imbecility in one of twins has been reported by Brousseau,[35] Halbertsma,[36] McLean,[37] Shattuck,[38] Clay,[39] Waring,[40] Armstrong,[41] Chown,[42] and others, and the general conclusion is drawn that the condition was the result of a defect in the germ plasm and not due to the race or general physical condition of the parents. Furthermore, if the cause or etiology were related to the condition of the mother during pregnancy, one would always expect the identical pathologic condition to be present in both twins. Thurston[43] was of the opinion that the importance of the age of the mother has been overemphasized. In a recent and very careful review and study of the etiology of mongolism, Jenkins[44]points out four possibilities, namely:

"1. Mongolism is a genetic character, the expression of which is dependent on the age of the mother. Potential mongolism may be transmitted as a genetic character, but the expression of the condition is in some fashion controlled by maternal age, such as through some nonrandom selection of genes in the reduction process (resulting in a deviation from the Mendelian ratios) or some differential viability of zygotes related to the age of the mother.

"2. The immediate cause of mongolism is a local pathologic change in the uterine mucosa. This would explain the monozygotic twins (which have a single placenta) and the fact that in the case of dizygotic twins only one member is affected. In this case the rationalization would be that only one of the ova was implanted on the pathologic locus.

"3. The etiology of mongolism is to be sought in a modification of the sperm cells by the toxic action of the secretions of the female generative tract, this toxic action being related to the age of the mother. This appears unlikely, but should be considered as a possibility.

"4. Mongolism is due to a diminished viability of the ova." In his conclusions Jenkins states: "(1) The relation of mongolism to twinning (both members affected in monozygotic twin pairs, one member affected in dizygotic twin pairs) substantiates the belief that the immediate etiology of mongolism is to be found in the germ cell. (2) The association of mongolism with a diminished maternal fecundity (increasing age of the mother, small size of the family and frequency of an abnormally long interval before the birth of a Mongolian idiot) supports the conception that the Mongolian idiot is a product of fertilization of an ovum, the viability of which is diminished. (3) The hypothesis that mongolism is due to a diminished viability of the ovum, short of complete failure of development, makes it possible to harmonize the superficially paradoxical evidence pointing toward the germ cell and maternal age as etiologic factors."

Recently attention has been forcibly called to the occurrence of this condition among the Ethiopian race by the increasing number of case reports appearing in the literature[45, 46, 47, 48, 49, 50, 51, 52] (Another fact which tends to disprove the proposed theory that there might be a

relation between this disturbance and the Mongolian race.) In one of the cases reported there was possibly an admixture of Caucasian blood which, if one still insists that the condition is peculiar to the white race, might explain its occurrence. However, the frequency with which this disorder is being noted in the negro race certainly suggests that it is not peculiar to any one race. During the past year the author had the opportunity to see a typical case of mongolism in one of negro twins.

The diagnosis can usually be made at birth, although occasions may arise when it cannot be definitely recognized until the sixth month of life. However, the almond-shaped eyes with epicanthal fold, the facial grimaces, fissured, pointed, and often protruding tongue, short hands with "fish-hook" little finger, generalized hypotonia, and the short foot with widely separated great toe usually serve as adequate diagnostic evidence to differentiate from that condition with which it is most frequently confused, namely, cretinism.[53] Penrose[54] has pointed out an interesting and helpful abnormality in this group of patients and one that is essentially peculiar to this form of imbecility alone. This consists in the presence of only two creases in the little finger instead of the usual three, although all three phalanges are present, i.e., the creases in the little finger of the Mongol resemble those of the thumb of a normal person. These children are happy, placid, affectionate, and good-humored. Their mentality varies from complete idiocy to feeblemindedness, the majority belonging to the imbecile group.

Encephalographic studies in these patients have shown deep subarachnoid spaces with widely separated convolutions and deep sulci. The ventricles are usually evenly and symmetrically dilated. Davidoff,[55] in a careful study of the brain in mongolism, found "few morphologic changes are constant, with the exception of: a small cerebellum and brain stem, the embryonic convolutional pattern, and my own observation of the small content of ganglion cells of the third cortical layer." He concluded the brain in mongolism showed (1) agenesis, (2) aplasia, and (3) paragenesis.

Treatment of this disorder is of no avail and although there is an increase in metabolism and general activity following the administration of thyroid extract per se or polyglandular extracts, this increase is only temporary. However, whenever there is any doubt as to the diagnosis, the administration of *adequate* doses of thyroid extract is justifiable, for there is the possibility that one may be dealing with cretinism. Once the proper diagnosis is established the further administration of this form of therapy does not seem warranted.

To summarize briefly the present situation in this disorder, one might quote the conclusions of Whitney,[56] et al.

"(1) The etiology is obscure.
"(2) There is a wide variation of physical characteristics.
"(3) The Mongol is capable of but slight mental development.
"(4) The diagnosis should be made in infancy.
"(5) The prognosis at best, from any angle is poor."

POLIOMYELITIS

Mathers[57] in 1916, published a preliminary report concerning the etiologic agent responsible for poliomyelitis and described a micrococcus isolated from the cord and brain of such cases. At first he was

of the opinion that this was purely a secondary invader, but subsequent studies[58] led him to believe it might be an important factor. Since his observations the literature has contained a large number of publications both confirming and denying this possible relationship. Rosenow,[59] who has been the strongest advocate of this theory, has described a pleomorphic, green-producing streptococcus which he feels is the causative factor. In an effort to confirm his views further a precipitin test[60] to detect the presence of the organism, as well as a skin test to determine the patient's susceptibility,[61] has been introduced. Antistreptococcus horse serum[62] has, in his hands, not only shown neutralizing powers in experimental poliomyelitis but has also proved of value as a therapeutic agent in the treatment of the disease.[63, 64] Rosenow has also reported several outbreaks of the disease that were apparently due to infection from this organism. His most recent report[65] concerned an epidemic that occurred at White Bear Lake, Minnesota, and in his summary he states: "The etiologic importance in acute epidemic poliomyelitis of streptococci having characteristic cataphoretic velocity and virulence and specific antigenic properties, that have been described repeatedly previously, is again emphasized by the results of this study." Bull,[66] in 1917, after a very careful investigation of the pathologic effects of streptococci on rabbits was unable to confirm Rosenow's results. Long, Olitsky and Stewart[67] later confirmed Bull's observations and similar results were obtained by Kolmer, Brown and Freese.[68] At the present time the more commonly accepted theory is that the disease is due to a filtrable virus.

The exact *incubation period* of poliomyelitis has been difficult to determine and at present the majority of the data employed to determine this interval have been obtained from animal experimentation, cases of known exposure, and the occurrence of multiple cases in the same family. Wemstedt[69] has concluded that the period ranges between four and seven days, seldom less than four and rarely more than twelve; Aycock and Luther[70] have placed it as varying from six to eighteen days. Likewise, difficulties have been encountered in determining the period of infectivity or contagion. Wilson[71] is of the opinion that the infectivity is at its height during the incubation and preparalytic stage; Knapp, Godfrey and Aycock[72] have presented evidence to show that the infection may be transmitted during the incubation period, and other authors have reported the recovery of the virus during the acute stage, the period of convalescence, or several months later.

Peabody, Draper, and Dochez[73] in 1912, strongly advocated that poliomyelitis was a general systemic disease. In 1917, Draper[74] further emphasized this view and again in 1931.[75] As a result of animal experimentation Fairbrother and Hurst[76] in 1930 drew attention to the possibility of axonal spread, and further impetus was added by the work of Jungeblut and Spring[77] who, after transecting the spinal cord of a monkey, inoculated the animal intracerebrally with the virus and were subsequently able to demonstrate typical pathologic changes above the site of transection but no changes below the lesion. In a recent publication, issue has been taken with the theory that poliomyelitis is first a "systemic" or "general" infection, before it involves the central nervous system. The purpose of Faber's[78] publication can best be stated in his own words: "It is to the purpose of

examining the pathology and symptomatology of the human disease in connection with the point of entry of the virus and with the anatomy and functions of the central nervous system to see how well the axonal theory harmonizes with the facts; to attempt a reinterpretation of the clinical course in its light, and to discuss certain changes which it involves in our attitude to some of the problems still awaiting solution, that the present paper is devoted."

Faber very carefully and painstakingly attempts to present a composite picture of our present knowledge of the disease, offers a very interesting explanation for the mode of propagation of the virus and at the same time associates the clinical manifestations and the pathologic changes. Space does not permit a full abstract of this paper, so only the conclusions will be quoted:

"Poliomyelitis throughout its entire course is primarily and essentially an infectious disease of the central nervous system, caused by a strictly neurotropic virus. Only when it is so regarded can its various clinical and pathologic manifestations and the results of experimental investigation be harmoniously correlated and interpreted; and only then do the inherent contradictions and obscurities of previous conceptions of the disease begin to disappear. The idea of a "systemic," extranervous phase preceding invasion of the central nervous system must be abandoned.

"The clinical course of the disease has been shown to correspond with the advance of infection through and within the central nervous system, and a consideration of the portal of entry (olfactory mucosa), of the distribution of the lesions, of the anatomy of the nerve tracts, of the character and chronological order of the symptoms, leads to the conclusion that the infection follows a fairly well-marked main route from the upper olfactory centers to the site in the anterior horns of the cord where it produces its most marked and disastrous effects. This route leads through the olfactory nerves to the olfactory bulb; through the olfactory tracts to the interbrain (hypothalamus and thalamus), where it often excites early symptoms; through the spinothalamic tract to the posterior horns and intervertebral ganglia of the cord, where it produces the later preparalytic symptoms; and thence to the anterior spinal horns. The main reason for believing that the infection descends along a sensory tract to the posterior horns rather than along motor tracts, such as those with relays in the midbrain, is the fact that in nearly all cases of poliomyelitis the sensory symptoms—predominantly pain, either spontaneous or on manipulation—precede the motor symptoms. A second route leads from the hypothalamus to the medulla. Since in the average case bulbar symptoms are absent or slight or transient, and since the main sensory tract leading from the medulla to the cord is apparently rarely affected, this route is regarded as being a subsidiary one.

"In principle, the mode of propagation is by implantation and multiplication of virus in the ganglionic cell centers along the route with passage from one center to the next through the axones of the connecting nerve tracts, according to the hypothesis of Fairbrother and Hurst. The tendency of the virus to die out in those centers where conditions for its survival are not optimal offers an explanation of the frequent occurrence of interruptions in the clinical progress of the

disease (phenomenon of 'halting'), the most striking instances of which are the 'dromedary' phenomenon and the nonparalytic ('abortive') case.

"In accordance with the general conception of the disease as above outlined, its course may be divided into four successive stages or phases which are sometimes separated by intervals of symptomatic silence and sometimes occur in such rapid sequence that there is apparent overlapping.

"It is possible that the classification shown here may increase the facility of diagnosis by drawing more attention to the earliest manifestations of the disease, particularly the psychic, sensory, and vegetative symptoms, and bringing their significance into better focus. It is to be hoped that better cooperation of the neuropsychiatrist with the pediatrician and internist may be obtained in the future with the object of studying and defining the early symptomatology with greater precision.

"If, as is theoretically possible, the tendency to 'halting' in the progress of the disease is due in some part to contact in the tissue spaces between circulating viricidal substances and virus passing from one neurone to the next, this would suggest the mode and technic of treatment which promise to be most effective. The essential features of such treatment would be: use of serum of known high neutralizing power; maximum safe dosage and intravenous administration to obtain the maximum concentration of antibodies in the blood stream at the earliest possible moment. Treatment as at present generally practiced fulfills none of these requirements. Intrathecal administration, without simultaneous use of intravenous hypertonic solutions is theoretically inadequate since serum so administered is unlikely to regurgitate at all or for more than a very brief time into the perivascular and perineuronal spaces against the normal direction of flow of fluids in these channels which, in addition, are largely blocked by infiltrations of small cells. On the other hand, serum administered intravenously would be favored in reaching the affected cells and tissues by the normal direction and conditions of flow from the capillaries and, in addition, by the conditions of increased blood flow and vascular permeability resulting from the inflammatory reaction existing in the affected parts."

Seasonal incidence,[79, 80] age distribution,[81, 82] and immunity,[83, 84] have been so thoroughly discussed that a review of these factors would only be repetition. Furthermore, the occurrence of multiple cases in the same family,[85, 86] the anthropologic features,[87, 88] the blood groups,[89] and symptomatology[90, 91, 92, 93, 94, 95] do not warrant discussion at this time, as the literature is both adequate and voluminous.

Treatment.—"The initial symptoms are much the same in all types of the disease and they may be quite as severe in the nonparalytic as in the paralytic."[96] This statement by Neal shows very clearly how difficult it is to determine the efficacy of any form of therapy instituted during the preparalytic period of acute poliomyelitis. Furthermore, it is impossible to evaluate properly the results of a given form of treatment unless the results can be compared with properly selected and supervised cases that did not receive treatment. The great difficulty in determining the value of convalescent serum (Technic of obtaining and preparing serum[97]) has been the lack of control cases.

Soon after the introduction of this procedure in the treatment of acute preparalytic poliomyelitis, the literature contained favorable reports[98] and one received the impression that convalescent serum was of definite value. However, the only controls were those cases diagnosed after paralysis had appeared and these patients in many instances, were not seen prior to that time. Obviously, herein lay an actual error in drawing conclusions, for the number of patients who recovered *without* paralysis and who were never seen, could not be included. In fact, the only conclusion that actually could be drawn from these early observations was that *if the serum were of value, it should be given early*[99] and before paralysis had developed. This same criticism, i.e., inadequate control groups, may be applied to the observations of recent authors[100, 101, 102, 103, 104, 105] who advocate the administration of convalescent serum. Andrews[106] has presented evidence to show that when a virus of the filtrable class has made its biologic union with the tissue cells it is no longer within reach of a neutralizing virus. This observation offers a possible explanation for the failure of the serum to be of value as a therapeutic agent.

Torian and Winters[107] are of the impression that convalescent serum is of little value in influencing the course of the disease, yet they treated only four cases during the preparalytic stage, and definite conclusions cannot be reached from such a small number of cases. In an extensive series of 927 preparalytic cases, 519 of which were treated with convalescent serum while the remaining 408 were not given serum, Park[108] found that paralysis developed in 19.6 per cent of the treated cases, in only 11 per cent of the untreated cases, and that the mortality rate among the former group was 3.8 per cent as compared to 0.9 per cent among the latter group. The recent observations of Kramer, Aycock, Solomon and Thenebe[109] in a carefully controlled series of treated and untreated cases also fail to give any statistical evidence of its value as a therapeutic agent.

In her conclusion on the treatment of poliomyelitis by convalescent serum Neal[110] states: "A group of more than 1000 cases, including those of Kramer and Aycock, diagnosed in the preparalytic stage, with approximately half treated by convalescent serum, shows nothing to indicate the therapeutic value of the serum, either in reducing case fatality or in preventing paralysis. Indeed, the slight difference between the treated and untreated groups is against the use of serum. Since the same results were shown by three groups of workers—the physicians of the Health Department and Hospitals, the physicians working under the direction of the subcommittee on Poliomyelitis of the Public Health Relations Committee of the New York Academy of Medicine, and Kramer and Aycock and their associates—it may be concluded that these cases were diagnosed and treated without personal bias. It is fair to say, however, that there is a belief that the percentage of moderately severe cases was a little greater in the treated children in the group studied under the direction of the Academy of Medicine." At the present time, further observations among carefully controlled cases would seem to be indicated before definite conclusions as to the specificity of action in preventing paralysis in this disease can be drawn.

Convalescent serum has been administered intrathecally, intravenously, and intramuscularly, either alone or in combination with one or more of the other methods. The intrathecal injection of the serum,

though advocated by some, does not appear advisable, for it is invariably followed by an exaggeration of the clinical manifestations of meningeal irritation as evidenced by marked discomfort of the patient. Furthermore, it is a well-recognized fact that the presence of serum of any nature within the cerebrospinal fluid establishes a sterile meningitis and thereby possibly increases the already existing reaction. The intravenous route is preferable, for in this manner large amounts of the serum may be readily administered and rapidly distributed throughout the body. If convalescent serum cannot be obtained and it seems advantageous to administer this form of treatment, a blood transfusion may be employed. Certain authors[111] have advocated this procedure over serotherapy, as a donor can usually be obtained without delay and larger amounts can be given.

The administration of convalescent serum, or whole blood, as a widespread prophylactic procedure has been advocated, but at the present time the scientific evidence is insufficient to warrant its acceptance as a universal measure. In view of the fact that the majority of adults have acquired an immunity[83, 84] to the disease whereas young children have not, it may be advisable to administer serum intramuscularly or intravenously to this group when a member of the family has developed the disease. This passive immunity, however, is only temporary, lasting from five to seven weeks, and should the person be reexposed after this period, a second injection of serum would have to be given. If such prophylactic measures were employed, many children would unnecessarily be subjected to treatment simply because a case occurred in their neighborhood.

The treatment of respiratory failure in acute anterior poliomyelitis by means of the Drinker respirator[112] has resulted in the saving of many patients who, it is reasonable to suppose, would have otherwise died. The first patient treated by this method was reported in 1929,[113] and since that time many additional reports have appeared.[114, 115, 116, 117, 118] The use of the respirator has been admirably discussed by Wilson[119, 120] who, in a study of 90 patients suffering from various types of respiratory embarrassment, has pointed out three mechanisms, each of which, or a combination of which, may produce these distressing symptoms; ". . . Three possible mechanisms were distinguished which brought about respiratory failure. The first, paralysis of the intercostal muscles or of the diaphragm; the second, in patients with pharyngeal paralysis, excessive fatigue caused by continual interference with inspiration by unswallowed material in the pharynx or to actual aspiration of this material; the third, direct involvement of the respiratory 'centers.' The treatment in each case must be planned for the type of respiratory embarrassment present. The best results with the use of the respirator are obtained in children with a high spinal type of paralysis, i.e., those with intercostal and diaphragmatic paralysis. In this group the prolonged and uninterrupted use of the respirator to avoid fatigue and dyspnea, and minute care of the patients in regard to the skin, fluid intake, and elimination, form the salient features.

The use of the respirator in cases with only bulbar paralysis does not seem logical unless the respiratory centers seem definitely depressed, in which case artificial respiration is sometimes of value. In patients with prolonged paralysis, treatment should be directed to postural drainage, aspiration of pharyngeal secretions (which at times

may require a tracheotomy), and to the avoidance of vomiting by withholding all fluid or food by mouth.

Obviously many patients are encountered who are suffering from paralysis of both the pharynx and the respiratory muscles and in these cases discriminating care and minute attention are prerequisites to successful therapy. Favorable results with the Drinker respirator have recently been reported by Smith[121] whose conclusions are in accord with those of Wilson.

Not only has the respirator proved of value in the treatment of the acute phases of the disease but also in the treatment of the residual respiratory muscle paralysis. Legg[122] states: "Measurements of voluntary expansion of the chest taken on a series of patients who received regular daily treatment in the respiration machine over a period of months, showed a definite and steady increase from amounts under one-half inch up to two and three inches of voluntary expansion away from the machine. It was noticeable that this expansion was produced mainly by the intercostal muscles as in a normal person, without the excessive use of the accessory muscles of respiration, such as the sternocleidomastoids, which, if present, were very strikingly used at first.

"From a medical standpoint, the increased aeration of the lungs and the deeper movement of the diaphragm in the abdominal cavity resulting from the use of the respirator should be an aid to the general health of the patient, in addition to its value in preventing deformities of the chest and in aiding the return of power to the muscles of respiration."

TUBERCULOUS MENINGITIS

In 1932 Bókay[123] reported successful results in the treatment of 5 of 17 cases of tuberculous meningitis (the diagnosis was established by both clinical and bacteriologic examinations) by energetic deep roentgen therapy. The author divided the cases into two classes, an exudative diffuse, and incurable group, and a local meningeal tuberculosis; it is this latter group that has responded to treatment. Wiener,[124] encouraged by the report of Bókay, treated 9 cases with roentgen therapy but was unable to obtain any improvement. In fact, it was his impression that the treatment hastened the death of the patients. However, some consideration must be given the fact that Wiener's cases were advanced while Bókay's were treated early in the course of their disease. Gordon[125] treated 3 cases by this method with the following results: "Two of them, according to the concepts presented, offered no favorable response to this method, in that the tuberculous infection of the meninges was only an accompanying part of a generalized miliary dissemination of the disease throughout the body. . . . The third patient was judged favorable for this form of treatment in that the infection of the meninges was the outstanding manifestation. . . . All three patients died, the first two rather promptly. The third one, the child being favorable for treatment, showed a well-marked clinical response early in treatment, with decreased fever, improvement of physical signs, and most important, improvement of the sensorium and general clinical appearance. A relapse occurred after six days with death on the eighth day." The extremely high mortality rate of this disease certainly justifies any therapeutic procedure which, in itself, is free from danger. Obviously further clinical investigation is warranted.

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American Academy of Pediatrics

Proceedings

THIRD ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

June 12, 1933

Round Table Conference on the Treatment of Nephritis

Leader: C. Anderson Aldrich; Assistants: Charles F. McKhann, Jr., and Alexis F. Hartmann.

DR. C. A. ALDRICH.—As originally planned, this discussion was to be on the subject of nephritis in general. Because this topic is so comprehensive, we shall limit ourselves more or less to therapeutic considerations of the three most common types of nephritis: acute, postinfectious hemorrhagic nephritis; nephrosis; and chronic nephritis.

In order to clarify the discussion, perhaps definitions of these conditions are in order. *Acute postinfectious hemorrhagic nephritis* is the common type seen in childhood, characterized by the elimination of grossly hemorrhagic urine, coincident with or following febrile infectious processes and a tendency toward edema and cerebral symptoms, usually leading to complete recovery in from 6 to 8 weeks. *Nephrosis* is a relatively rare type showing massive edema frequently in successive waves, marked albuminuria, absence of hematuria, high blood pressure, and blood nonprotein nitrogenous constituents and manifesting a decided tendency to chronicity. *Chronic nephritis* in dispensary practice, at least, occupies an intermediate position from the standpoint of frequency. It is characterized by edema, albuminuria, hematuria, hypertension, high nonprotein nitrogen values in the blood, and runs a markedly chronic, downhill course usually ending fatally within a few months or years. In all three, casts are found in the urine at times.

I will ask Dr. McKhann to proceed with the consideration of the acute disease.

DR. CHAS. F. McKHANN, BOSTON.—I propose to limit my remarks to a discussion of nephritis in childhood as it occurs after acute infections.

Although evidence of renal dysfunction, especially albuminuria, may become apparent in the course of acute infections, particularly those accompanied by considerable febrile reaction, the type of renal disorder observed at the fastigium of the febrile process bears no established relationship to the usual forms of nephritis in childhood, nor does febrile albuminuria usually precede the onset of acute glomerular nephritis.

Acute glomerular nephritis in its varying degrees of severity is the type of nephritis encountered most frequently in childhood and is the form of the disease preceded by acute infections, commonly caused by the hemolytic streptococcus. A period of several days to two or three weeks elapses between the onset of the acute infection and the time at which renal symptoms are noted. A child who has been ill with tonsillitis, otitis media, adenitis, or other infection may recover sufficiently to be up and about or even to return to school before slight edema under the

eyelids or the appearance of smoky, bloody urine directs attention to the renal condition. Hematuria persists for a variable period of time, usually unaccompanied by manifestations more serious than pallor, slight puffiness of the face, and some degree of anorexia. The distinctive smoky color of the urine is due to the presence of red blood cells which gradually settle out, forming a brownish sediment containing in addition to the erythrocytes many leucocytes and casts. Phenolsulphonephthalein excretion is normal, as well as the salt excretion. There is generally, however, diminished excretion of the end-products of nitrogen metabolism. The volume of urine is diminished in acute glomerular nephritis, sometimes to the point of anuria. Edema is present but usually not to a marked degree; frequently it passes unnoticed or is observed only as puffiness under the eyes. With improvement there is observed loss of weight, and increase in the volume of urine. The average duration of symptoms in our cases has been six weeks. Occasionally a more prolonged course is observed and perhaps more frequently a milder type of disturbance is encountered. Recently we have observed a number of patients who developed hematuria after acute infections, but in whom the renal manifestations subsided in from five to seven days. It appears probable that published statistics understate the incidence of acute glomerular nephritis because of the omission of these mild and transient forms of the disease.

It is interesting to note that age is a factor in the etiology of acute glomerular nephritis, the disease being rare under two years. Sex is unimportant, but season and climate affect the incidence in as much as both factors determine the frequency of the types of infection which precede the development of nephritis of this type.

The prognosis in acute glomerular nephritis is good not only as regards life but also as regards complete recovery. Transition to a chronic type of nephritis is uncommon.

In the course of acute glomerular nephritis there may develop a disturbing train of symptoms, referable to the central nervous system and not definitely related within wide limits to the severity of the renal lesion or to retention of the end-products of nitrogen metabolism. Vomiting, frequently of a projectile character, headache, visual disturbances, a slowing of the heart and respiratory rates, coma, convulsions, and death from central respiratory failure are encountered in this syndrome accompanying nephritis. This is often called uremia, although it differs considerably from the true uremia of terminal chronic nephritis. The systolic and diastolic blood pressures are slightly elevated in almost all cases of acute glomerular nephritis but in patients with cerebral manifestations, the blood pressure is elevated to a considerable degree and parallels in elevation and rapidity of rise, the severity of the cerebral symptoms. The systolic blood pressure in acute glomerular nephritis usually remains below 120 mm. of Hg. A rise above this figure indicates the development of cerebral involvement and with a blood pressure around 140/100 the patient usually complains of headache and may vomit.

The possibility of the development of coma or convulsions is indicated by continued rise of the blood pressure. Thus, an increasing systolic blood pressure assumes considerable importance as a danger signal, warning us of the imminence of cerebral manifestations. These cerebral symptoms are not peculiar to uremia of acute glomerular nephritis, but are the symptoms characteristically produced by a rapidly increasing intracranial tension. The presence of cerebral edema and increased intracranial pressure in this form of uremia has been amply proved at necropsy.

Of the therapeutic agents we have employed in the treatment of patients exhibiting cerebral manifestations with acute glomerular nephritis, magnesium sulphate has proved to be of most value.

Magnesium sulphate by mouth and by rectum suffices to control and relieve the cerebral symptoms if the administration of the salt is begun with the appearance of elevated blood pressure, during the stage of headache and vomiting, and before the development of coma and convulsions. Large doses of the drug are necessary; one to two ounces of 50 per cent solution every four hours are necessary to produce the desired results. As pointed out by Aldrich, magnesium sulphate administered to patients with acute hemorrhagic nephritis seldom causes diarrhea even when massive doses are used.

The action of magnesium sulphate seems to be one of general dehydration with resultant diminution of cerebral edema. Improvement is seldom obtained without loss of body weight, and is accompanied by a gradual fall in blood pressure.

In comatose patients or in those with convulsive twitchings, parenteral administration of the salt is necessary. Formerly we used a 1 per cent solution of the anhydrous salt intravenously. Prompt fall in blood pressure with accompanying relief of symptoms was obtained by this method of treatment. Subsequently we ascertained, however, that intramuscular injection of the salt had almost as prompt an effect in relieving symptoms and reducing the blood pressure, so we have not recently had recourse to the intravenous mode of therapy. For intramuscular injection a 25 per cent solution of the crystals of magnesium sulphate is used in a dosage of approximately 0.5 c.c. per kilo of body weight. This dose may be repeated in three or four hours if necessary to control symptoms. In some cases several repetitions of the treatment have been required before the blood pressure remained low and the cerebral symptoms disappeared.

The introduction of this form of therapy has almost eliminated fatalities among our cases of acute glomerular nephritis, inasmuch as the prognosis of the uncomplicated disease is good, and the menace of the cerebral complications is largely overcome.

Let us consider for a moment the prophylaxis and treatment of uncomplicated acute glomerular nephritis. We are helpless to prevent an attack of nephritis following infection. Hygienic and therapeutic measures such as rest in bed, forcing of fluids, restriction of diet and even specific measures such as serum in scarlet fever seem to have little effect on the incidence of the ensuing nephritis.

Ordinarily the child with acute glomerular nephritis should be kept in bed as long as hematuria persists. Restrictions of the diet are often enforced needlessly. So-called standard nephritic diets often are restricted to such an extent as to be distressing or harmful to the patient. To keep rapidly growing children on low protein, low salt diets with limited fluid intake has little beneficial influence on the disease and may result in injury to the general condition of the child. The child with uncomplicated glomerular nephritis may receive a moderately liberal diet and need have no restrictions placed on the fluid intake. Should cerebral manifestations appear, some limitation in diet may be desirable. However, anorexia accompanies the development of the train of symptoms and the patient will usually restrict his own diet. Fluids by mouth seldom need to be limited, even in the more severe cases. The administration of salt solution parenterally to a child who is accumulating edema fluid appears, however, to be contraindicated.

DR. ALDRICH.—I will ask Dr. Hartmann to open the discussion on nephrosis.

DR. ALEXIS F. HARTMANN (ST. LOUIS).—Since the etiology of lipoid nephrosis is as yet obscure, methods of treatment are necessarily directed against either a theoretical cause or certain symptoms of the disease. No attempt will be made to review the many treatments already proposed. Our own personal experience thus far with the disease has led us to adopt the following scheme:

If a tentative diagnosis of active nephrosis seems justified from the history, physical examination, urinary and blood findings, the patient is at once placed on a

high protein, high carbohydrate, low fat diet, with restriction of salt and water. Further treatment depends largely upon the response to this diet. If fairly prompt loss of edema by diuresis occurs, we consider the case mild, remove the restriction of water and salt, but continue with high protein feedings until the plasma proteins of the blood return to normal levels. At this stage, suspected causative foci of infection are treated surgically, if deemed necessary.

If the case is more severe and edema persists, we presume it is because of continued low plasma protein levels in the blood, and we then study the patient more intensively to ascertain:

(1) The exact concentrations of albumin and globulin and the actual or calculated oncotic pressure of the blood serum.

(2) The daily excretion of albumin in the urine.

(3) The actual intake of protein food and its utilization.

If we find serum protein and oncotic pressure values to be rather high in the edema zone, together with good intake and utilization of protein food and but a moderately severe degree of albuminuria, we then transfuse the patient, first with whole citrated blood until the red blood cell and hemoglobin values are normal, and then with plasma, in an attempt to raise the plasma protein level out of the edema zone. If diuresis does not take place, we may then try the effects of diuretic drugs and thyroid gland substance, but with much less hope of success. If failure persists, we judge the case to be in need of acacia therapy, a preliminary report of which has already been published.

In Chart I (lantern slide) we have presented graphically the course under treatment of our most recent case of nephrosis. The points of particular interest are:

(1) The very low initial values for serum albumin and oncotic pressure (as determined by Wells' method).

(2) The very rapid excretion of transfused plasma albumin, explaining why, in severe cases, loss of edema following transfusion is very improbable.

(3) The raising of the serum oncotic pressure out of the edema zone with gum acacia, and the subsequent diuresis with complete loss of edema.

(4) The gradual recurrence of edema following loss of acacia from the serum and

(5) The apparent good effect of gavaged feedings in helping to reestablish the diminished plasma albumin and to permit subsequent diuresis and recovery.

DR. ALDRICH.—I will undertake to summarize our experience in the treatment of chronic nephritis, but before considering therapeutic procedures one must know something of the clinical course of the disease. For over thirteen years I have studied this aspect of the problem and have collected over forty cases. With the help of especially competent social service follow-up, it has been possible to state definitely the ultimate result in all of these children. In general it may be said that in the early stages all of them presented all of the clinical signs and laboratory findings: Edema, hypertension, increase in the nonprotein nitrogenous constituents of the blood, hematuria, marked albuminuria, and cylindruria. If death did not occur during the first few months, these manifestations fluctuated widely in severity, tending toward progressive disability. After a period of years, renal insufficiency dominated the picture and death occurred from true uremia often complicated by marked acidosis, cardiac decompensation, and practically always with gross infectious processes, although these were usually absent during the major course of the disease.

The onset was usually insidious and not associated with typical postinfectious nephritis. Edema was most often encountered early, many patients exhibiting none after the first few months. This symptom was usually fairly amenable to a salt restricted regimen. Hypertension fluctuated widely but tended toward a progressive

increase. In a few instances sudden elevations were accompanied by cerebral symptoms, but this happened less often than in acute nephritis. There was also marked variation in the elevation of the blood nonprotein nitrogen, but this tended to rise markedly with severe renal insufficiency. The hematuria was not always present, but was found at some time in every patient. The fact that blood may be absent from the urine for months or even years may lead to confusion in the diagnosis, but should not if other observations and the history are carefully considered. Albuminuria is a constant observation. In none of my cases did it come and go as is so often stated. Renal function tests show early and progressive impairment as a rule.

Consideration of some of the above features of the clinical course have influenced our management of the patients. When we noted that only an occasional patient with chronic nephritis gave the history of acute postinfectious nephritis at the onset, and that even the patients most severely ill with postinfectious nephritis usually made complete and permanent recoveries, we began to doubt that we were dealing with identical processes. It seemed possible that the pathologic lesion in postinfectious nephritis might be of a more benign nature than the progressive sclerosis found in chronic nephritis. We began to think of this latter as a separate clinical entity and attempted, we think with considerable success, to differentiate it before chronicity alone established its nature. This attitude made it necessary for us to look for some cause other than microbic infection, and in casting about, we noticed that almost all reported cases were found in dispensaries, that the disease is a clinical rarity among the well-to-do. Moreover, the patients were malnourished and surrounded by poor hygienic environment.

In the fall of 1930, having arrived at this stage in our observations, we were faced with a serious problem. The morale of the clinic was at a low ebb. All of the patients were receiving a low protein diet and many were forced to eliminate salt as well. Almost all were clinically ill and obviously dying off in spite of our good intentions. They were an unhappy, miserably ill group of children. It was no pleasant duty to go on week after week and watch this process complete its degenerative course. Doctors, nurses, social service workers, and patients had no heart in the job.

Therefore, in October, 1930, we resolved on a radical change. All preconceived ideas of diet were discarded and we decided to treat these children exactly as we would any other group in as poor a nutritional state; to make every effort to improve their nutrition and physical and mental hygiene. The following reasons were responsible for the decision: (1) The disease manifested some of the evidences of a nutritional, hygienic, or deficiency disease; (2) our previous treatment had been futile, if not actually harmful; and (3) we hoped to make the remaining months or years of the patients' lives more endurable by giving them the satisfaction of eating palatable food just as other folks.

The following measures were taken. All patients were put upon a diet which we hoped might compensate for any deficiency. Meat or eggs were ordered three times daily, salt was allowed to all those who were not definitely edematous, and all the vitamins we had ever heard of were included in their diet. Cod liver oil, yeast, orange juice, and raw and cooked vegetables were prescribed. Wherever this could not be accomplished at home, we invoked the help of charitable organizations or took the patients into the hospital. In addition to this, every effort was made to improve the general hygienic environment of the children, including sunbaths in the summer, fresh air, etc.

While this was undertaken with some slight misgivings on account of precedent, we did not feel too guilty on account of the ten years of experience we had had on the regime prescribed by precedent. The results following the change were so

rapidly noticeable, however, that within three months doubt changed to surprise. All of the patients began to look better, and one returned with specimens of urine which were, and have since been, constantly free from albumin. Since that time two more have become albumin-free, a pleasure we had never before experienced. One by one the children became able to re-enter school. Hemoglobin estimations rose along with the weight curves, and this without edema. Clinical improvement in general health was noted within a few weeks.

With still greater satisfaction we found that neither the blood pressure nor the blood non-protein nitrogen values rose with this change. In fact, in many instances the tendency was toward a decline. While the albuminuria continued in most children, it tended to decrease in amount and disappeared entirely in three instances. The red blood cells have disappeared in eleven of fourteen living patients and casts are now a relatively rare observation among them.

Of the ten patients put upon this regime in October, 1930, only two have died. While apparently improving, these left our care and were put upon low protein, salt-free diets in other institutions. One died under such treatment, and the other returned to us in a moribund condition to die with acidosis and true uremia.

We have now under observation in the dispensary fourteen patients, twelve of whom have been receiving this diet for about two years. All are attending school regularly. With one exception all are in excellent nutritional state, and the weight, hemoglobin, and tissue turgor are good. The one child who is not in good condition was in desperate shape before the new regime was instituted but has been able to resume school work despite his severe nephritis. He is the only patient in this group who shows a progressive loss of renal function.

As a result of two years' experience with this dietary and hygienic regime we feel we can report that the majority of our patients have shown definite clinical improvement, that four have shown complete disappearance of clinical evidence of the disease, that one is continuing the downward course at a retarded rate, and the death rate has been decidedly reduced.

DR. R. J. SCOTT, JR. (LOS ANGELES).—I would like to ask about acacia. What preparation of acacia is used and what is the size of those ampules?

DR. HARTMANN.—We started by making acacia ourselves. We found it a rather difficult task to make a solution anywhere near as good as some of the commercial solutions, so that we are now using commercial acacia. The first commercial acacia we used was that ordinarily used for shock therapy, sterile 30 per cent acacia solution, containing 4.5 per cent sodium chloride.

Because we do not wish to restore a diminished blood volume with fluid from without the body, but want to pull in water from the edematous spaces, we do not dilute this acacia six times as recommended for shock therapy but use it either as it comes in viscous solution, which is hard to give, or dilute it with one or one-half volumes of distilled water, to permit it to flow more readily by gravity.

The high salt content of this material sometimes gave rise to a marked thirst during and immediately after the injection. It also caused febrile reactions sometimes. We then had some acacia made without any salt in it and we gave that in approximately 15 per cent solution, just thin enough to flow by gravity through the ordinary intravenous set. This was not followed by the usual thirst as with the salt acacia, still it occasionally gave rise to febrile reactions and we felt it was not so stable without added salt. We had some special acacia made, 30 per cent acacia containing 1 per cent sodium chloride and the usual procedure is to add 50 c.c. of water to a 100 c.c. ampule of this acacia and inject it very slowly by gravity into a vein. The usual dose as given is about 1 to 2 grams of acacia per kilo, ideal body

weight. I think the essential thing is to give it slowly; if it is given too rapidly, the blood volume is increased too rapidly which causes headache and sometimes vomiting.

It is important to see just what effect it has from the standpoint of efficacy on the oncotic pressure. If a method of determining oncotic pressure had not been available in our last case, we would probably have stopped the acacia administration too soon as it looked as though we were not going to get a diuretic response. Administration of acacia was continued, however, until the oncotic pressure exceeded 20 cm. of water and then diuresis resulted.

You can use the material containing 4½ per cent salt satisfactorily, but I would use less of it in a given dose, to avoid the extreme thirst and the likelihood of temperature reaction.

We have been trying to find out more about the effect of acacia on the liver recently and we have both dogs and rabbits to which we have given acacia, not only intravenously but intraperitoneally and subcutaneously. We have never given it in any other way than by the intravenous route to human beings.

DR. E. E. MOODY (JOPLIN, MO.).—Does the intraperitoneal administration of acacia produce any peritoneal symptoms?

DR. HARTMANN.—No, we have given about as much acacia intraperitoneally to rabbits, as we gave intravenously to our last patient, without producing peritoneal symptoms.

DR. SCOTT.—You have not given it to children intraperitoneally?

DR. HARTMANN.—No, we would not attempt to without being sure it would be absorbed and cause no harm.

DR. ALDRICH.—There is a decided likelihood it would not be absorbed subcutaneously on account of the edema, is there not?

DR. HARTMANN.—I should expect that edema would interfere with its absorption.

DR. J. E. HARVEY (PASADENA, CALIF.).—Is it possible that in the smallest dosage it might give rise to some disturbance in the liver, particularly after some time had elapsed?

DR. HARTMANN.—I do not know whether or not such trouble should be expected. There have been many surgical patients that have had acacia in the last fifteen years (since its introduction during the war), who seem to have recovered after its use and have had no ill effects. I think what will happen is just what happens to other colloidal substances like colloidal iron; probably a part will be taken up gradually by the liver and then released and excreted into the urine. Within the first two weeks as a rule, some 40 or 50 per cent can be recovered in the urine but when very large doses are given, that still leaves a lot to be accounted for.

DR. E. E. MURPHY (SALT LAKE CITY).—I should like to ask Dr. Hartmann if he has had any case of apparent spontaneous recovery in infants under a year of age?

DR. HARTMANN.—No. During the past ten years, we have had about fifty cases that proved to have nutritional edema. Spontaneous recovery in these infants has, of course, been seen frequently. That is why we have emphasized that we would hesitate to attribute a curative effect to any single dietetic material, drug or

thyroid extract. This lantern slide shows the spontaneous exacerbations and remissions in an untreated case in which we found the sequence of events always as follows: Previous to the exacerbation of the edema, we would find an increase in albuminuria, followed by a fall in plasma albumin. When the latter became low enough, edema would follow. On the other hand, before periods of diuresis, albumin would first diminish and then the plasma protein level would rise. Just what causes such fluctuations in the intensity of the albuminuria is as yet unknown. In some cases infection plays an important rôle.

DR. McKHANN.—Is it not true that infections vary in their effect? In some they cause edema to disappear; in others, to accumulate. It seems that when a patient gets measles, edema fluid promptly runs out. That is one disease in which we feel there is a disappearance of edema.

DR. HARTMANN.—We also have observed that, and have gathered enough information to explain, at least in part, some of the variable results.

This is the explanation: In the first place, if you want to correlate edema with plasma protein values, it is very necessary to consider the state of the edema; increasing edema will be associated with the low values, stationary edema with higher values, and the state in which the edema is being lost, with values that are still higher. If you take a single instance in which the protein level is high in the edema zone, and in which an infection has been followed by loss of weight, the weight loss may have been due in part to increased evaporation of water, in part to further water loss by vomiting and diarrhea accompanying the infection, but also to the following. As the patient recovers from the infection, the recuperative powers which we see working at their utmost following recovery from infection, seem to increase the rate at which the protein is made, so that even if the loss of protein in the urine continues unaltered, the level of plasma protein is elevated. Such "over-shooting" during convalescence is common as regards nutrition.

DR. McKHANN.—What about the observations during the infection?

DR. HARTMANN.—We have seen the tendency by poor protein intake worse during infection; that is explained by poor protein intake and reduction of nitrogen absorption because of vomiting and diarrhea. Just as soon as vomiting and diarrhea stop in such patients and they take in the usual amount of salt and water, edema may increase at a rapid rate.

DR. ALDRICH.—I think that is one of the most interesting subjects brought up today. In our series of patients with nephrosis we have had five who made spontaneous recoveries immediately following high fevers and the fevers were due to various diseases in the upper respiratory tract. Not only the edema, but also the albuminuria disappeared. These patients are still well today and not one of the five has had a relapse.

DR. HARTMANN.—With that in mind, we have tried to reproduce such spontaneous recovery a number of times by artificial fever produced by vaccines injected intravenously without results. It is the infection itself which does something toward the recovery and not the fever.

DR. ALDRICH.—Did you fail to get a response because you could not get reactions or because they did not get well? We have been unable to produce satisfactory fever in nephritic patients despite massive doses of vaccines.

DR. HARTMANN.—We secured febrile reactions with both streptococcus and typhoid vaccines.

DR. McKHANN.—In edematous patients with acute glomerular nephritis, we have not used the high protein diet.

DR. HARTMANN.—One has to consider the edema of acute hemorrhagic nephritis due to both renal and extrarenal factors which are not necessarily present in chronic nephritis or nephrosis. I think in acute nephritis with glomerular damage there is a very definite renal block. If water is put into such patients with little or no kidney activity, it has to go somewhere and it accumulates as edema fluid. This edema fluid is different from the fluid in chronic nephritis or nephrosis in that it has a much higher protein content, due to the effect of the toxin on the endothelium of the capillaries, which becomes more permeable to protein. Although it is difficult to secure subcutaneous fluid, one can easily get ascitic fluid. Appreciable amounts of protein are found in this fluid, very much more than you find in that of nephrosis. So there seem to be two factors working. There is definitely a block which is probably due to a poor circulation through the kidneys, plus the general effect on capillaries, which allows protein to pass through too readily. Any protein in the edema fluid is going to tend to hold water there.

DR. McKHANN.—I think the edema of acute glomerular nephritis is intracellular, rather than intercellular, and for that reason it is difficult to secure edema fluid for study.

DR. HARTMANN.—The oncotic pressure of the protein in the edema fluids in intercellular compartments and the peritoneal cavity is usually very little as compared with that of the plasma proteins, so that one would not expect much accumulation of edema. As far as colloidal osmotic pressure is concerned, edema begins at about 20 cm. pressure of water and extends on down. If the pressure is over 20 cm., we do not expect to find edema; under this figure we do. Normally the oncotic pressure is 30 to 35 cm. of water, so that there is considerable margin of safety. Unless the plasma oncotic pressure is much reduced, small amounts of protein in the edema fluids will not have much effect in increasing water retention.

I think one can produce a real hydremic plethora when there is renal block, so I do not see the reason for forcing fluids in the edematous stages of acute nephritis. It is all right, I think, to give water, milk, or fruit juices, but I do not see the need of forcing such fluids.

DR. ALDRICH.—I do not advocate actual forcing, but we do urge the patients to take fluids. While I believe we are in real agreement on this point, I would like to emphasize the fact that we are particularly anxious that patients with acute nephritis take plenty of fluids regardless of the amount of edema, and even in the presence of anuria. We feel it is quite likely that the urine is not excreted because water is not chemically available for secretion in such cases, and we do not see how diuresis can set in without its adequate administration. In our experience with over 200 patients with acute hemorrhagic nephritis only one has developed anuria when fluids were freely given. The only patient in the last ten years who has died of acute postinfectious nephritis in our hospital was on a regime of restricted fluid intake. We do not fear edema, but we do respect toxic symptoms. It is possible that extreme edema may have a marked detoxifying effect through dilution. I feel that it is as important to give fluids to toxic nephritics as it is to give antitoxin to patients with diphtheria.

DR. SCOTT.—Can you tell us more about oncotic pressure?

DR. HARTMANN.—I shall be very glad to take that up. We were supposed to talk only on treatment, so I did not attempt to explain oncotic or colloidal osmotic pressure.

What we refer to as oncotic pressure, other people refer to, perhaps a little less correctly, as colloidal osmotic pressure. What it amounts to is this: If serum is separated from Ringer's solution by a collodion membrane (impermeable to the plasma albumin and globulin, and to that extent then resembling the endothelial lining of the capillary), one finds that water from the solution tends to go through the collodion membrane into the serum which increases in volume, due to attraction by the proteins. This attractive force is the colloidal osmotic or oncotic pressure, which is allowed to manifest itself, because the membrane in this instance, the collodion sac, is impermeable to the plasma colloids, the plasma albumin and plasma globulin. You can measure such a force by putting hydrostatic pressure on the serum and finding out how much pressure is required to prevent water from coming into or leaving the serum. That is the colloidal osmotic pressure which is perhaps better referred to as oncotic pressure, because something more than osmotic pressure seems to be involved. In normal blood plasma it amounts to 30-35 cm. of water. The edema zone is quite wide, beginning usually around 20 cm. and decreasing.

DR. ALDRICH.—What do you use for a membrane in this method?

DR. HARTMANN.—Lately we have been using the method of Wells. Before that, we used something very similar to Govaerts' technic, using flat cellophane disks, but this recent method of Wells we find much more satisfactory.

DR. HARVEY.—I think Dr. Aldrich's paper is extremely interesting. It is a common sense method, because the child's natural reaction is to get well.

DR. HARTMANN.—Dr. Aldrich, in that connection don't you still feel that it is important to look for and treat, and possibly remove persisting infection? Don't you think the effect of diet perhaps works in this way: in the first place, the chronic nephritic on a protein-poor diet tends to get edema and if he is edematous, circulation, digestion and absorption all are interfered with; also, if he has a poor diet, resistance to infection is probably less. What you are doing is creating the best possible conditions for the patient to get over his infection spontaneously. It seems to me, however, that it is still necessary to look for and treat foci of streptococcic infection.

Until Dr. Dean came to the St. Louis Children's Hospital we had been missing one important site of infection. Looking back over our records we found there were good full notes on faucial and pharyngeal tonsils and on the paranasal sinuses, but almost nothing on the lingual tonsils. We then found a number of patients who had had their faucial and pharyngeal tonsils removed and their sinuses treated, but who still had infected lingual tonsils, which were successfully treated surgically or by diathermy.

We cannot say we cured patients of their chronic nephritis by such procedures, but from the findings, we certainly feel there was a good effect on the degree of hematuria, and in some instances even on the blood pressure, following the removal of such infections.

DR. ALDRICH.—I do believe infections should be eliminated. I think that in any patient with a disabling disease, every focus of infection should be cleared up. But our experience was identical with yours, in that we took out and drained all diagnosable foci, and still did not cure our patients. They were sometimes a little better, and recrudescences a little less severe, but we could not see that we had cured any patient of chronic nephritis by these methods.

DR. HARTMANN.—Perhaps another factor is coming into play. Your patients are now beginning to resemble more the adults that have been described by Addis and Van Slyke, and others. That is, for some years, both Addis and Van Slyke,

in their studies on glomerular nephritis have made the statement that the duration of chronic active glomerular nephritis might be from a few months, in the rapidly progressive cases, to quite a number of years, up to five or ten years. That is most unusual in children, is it not?

DR. ALDRICH.—We have had several of that duration.

DR. HARTMANN.—Did they last that long before you started feeding them?

DR. ALDRICH.—Yes, in some instances. Most of them died in a few years, however.

DR. HARTMANN.—What we want to know is whether the renal lesion really stops or merely quiets down and progresses at a slower rate. Another question is, just when do you call patients chronic nephritics? What marks the change from acute to chronic and where does the latency come in?

DR. ALDRICH.—We do not feel that there is any change from acute to chronic. At the present time we think we can distinguish the symptoms of the chronic disease from those of the acute before the chronologic factor decides the issue. In the majority of instances we are able to do this. The insidious, noninfectious onset and marked early impairment of function, especially the low fixation of the specific gravity of the urine, speak for the chronic type. I have never observed latency of nephritis in children. We consider the disease active as long as there are any abnormal physical or urinary abnormalities demonstrable. It has been our experience that once these have *all* disappeared, the disease does not again manifest itself, and we feel we can ascribe some weight to this statement because we have observed hundreds of these children for many years after their acute symptoms were over in our follow-up clinic.

DR. HARTMANN.—I am sincerely impressed by Addis' concept, which has been adopted also by Van Slyke, in this respect. I think it is extremely helpful. In this scheme, we expect about three-quarters of the acute hemorrhagic nephritics, which Dr. McKhann talked about, to get well within a few days or within a few months. If anything is left in the kidney, it is a scar, but it is healed.

A very few patients, not more than 5 per cent, progress rapidly, so that in a few months' time they reach the terminal stage of nephritis, which represents the picture Dr. Aldrich gave you, just before death. A few die before they reach that stage, from the more immediate effects of infection, such as acute myocardial damage or sepsis.

The remainder may lose all the physical findings of nephritis, and become latent nephritics; that is, they look normal, their blood pressure is normal; they are not anemic, their nutrition is normal, and the only way you can discover they are latent nephritics is by examining the urine, and sometimes only by the Addis method of concentrating the urine to keep the red cells from laking and to keep the casts from dissolving. Many of these latent nephritics in the course of months or years become healed; that is an observation everyone has made. Occasionally they have an exacerbation, and become acute. These again may become latent and healed, but some of the acute, as well as a number of the latent, continue to progress. In addition to the urinary findings we have just mentioned, they show other findings one can recognize, such as edema, anemia, malnutrition, hypertension, etc. They then are called chronic active nephritis. This is the serious group. How many of these do not progress to a terminal nephritis in the course of a year or two? Addis points out that only three out of his entire number of cases once diagnosed as chronic active hemorrhagic nephritics who became latent and healed; three for Addis and one for Van Slyke. That is a very small number.

Was Dr. Aldrich talking about the chronic active group or the latent group? If he had a high percentage of recoveries in this chronic active group, it is very remarkable; if they were in the other group, it is not so remarkable.

DR. BENGT HAMILTON (CHICAGO).—In that type of disease, as Dr. Aldrich said, the cases do not start with infection; the onset is often insidious.

DR. HARTMANN.—Have you ever followed them from an insidious start through to the development of a chronic nephritis? This is true in adults; you cannot always get a history of infection in the chronic stage and this was recognized and discussed by Addis and Van Slyke.

We had a patient who was to be discharged from the hospital following an acute infection. On this day a student checked his urine, found albumin and red cells and the discharge was cancelled. A typical mild attack of nephritis followed, lasting two weeks. Such an event could never have been discovered by any history. It is quite possible that a more severe attack could also have occurred without one's knowing it.

DR. ALDRICH.—Two or three things you have brought up are interesting. In the first place, mention of adult nephritis raises the question of whether or not the growth factor is of significant import in nephritis. I have watched several children grow up with chronic nephritis. As they have gone through adolescence there has seemed to be a definite change in the type of findings, more arterial changes were noted. One must be extremely careful in carrying over the observations of adults into a consideration of childhood nephritis.

Our histories have been carefully checked and we have seen several patients from the beginning of their apparent insidious onset. Of the forty patients we had with chronic nephritis, we could find a definite history of infection at the onset in only six. On the other hand, of our entire series of nephritics of all types, there were about thirty who gave no history of fever at the onset. Only five of these are well today, and we believe that in these five signs of infection were missed. Moreover, we have followed over 200 patients with postinfectious nephritis for many years, and I believe that no one of these has developed chronic nephritis. If any of them are latent, examination of the patients and urines has failed to reveal it. We have seen many patients after postinfectious nephritis show abnormal urinary findings for many months or a year or two, but these have all completely recovered eventually. This is not true of patients with the clinical symptoms we have described under chronic nonspecific nephritis.

That brings up the question of when a patient is cured. In the literature it is stated that the albumin comes and goes in the children with chronic nephritis. That has never been our experience. In these patients we have made many thousands of urinalyses and only a very few have ever been negative for albumin, so few that mistakes in technic or identity are the most likely explanation. Patients with chronic nephritis constantly show albumin in the urine, and negative specimens are a great rarity.

DR. HARTMANN.—The same thing is true of red cells and casts.

DR. ALDRICH.—The cells and casts have disappeared from the urines of our patients under our recent treatment long before the albumin was gone.

DR. HARTMANN.—Again and again we have felt that a patient had no blood in his urine, when, by collecting a concentrated twelve-hour night specimen, following a day of nonfluid restriction, we have found as many as fifty million cells.

DR. ALDRICH.—We have done benzidine tests routinely to check doubtful observation of red cells.

DR. HARTMANN.—That should show blood.

DR. ALDRICH.—I feel that this is a question which can be solved in only one way, and that is by continuous clinical observation on a large series of patients; it cannot be settled by statistical methods.

DR. HARTMANN.—That is the way I feel. Longcope had forty patients with glomerular nephritis and he obtained a clear-cut history of preceding infection, or found the infection with cultural evidence in 85 per cent of these, during the acute stage and most of these were due to hemolytic streptococci. Of these forty, he was able to follow twenty-two. Twelve recovered completely, which is a lower incidence than McKhann or we have seen in children. It may be due to the thing you mentioned, the growth factor.

The interesting point was that in eleven of these twelve, coincident with the recovery of the nephritis, the infective organism disappeared from the nose and throat and he was no longer able to culture these streptococci from the nose and throat. Whereas, from those who developed from active to chronic disease, he found clinical and bacteriologic evidence of persisting infection. It is true they were adults but I attach a good deal of importance to the figures and they were very well controlled patients.

DR. ALDRICH.—We have seen that happen and also have seen the nephritis clear up in the face of active mastoid infection. We have a patient in the hospital now who had nephritis and an empyema. After the chest was drained, the nephritis disappeared completely as far as we could tell. At the present time, he is still running a septic temperature up to 105° every day and probably has a persistent pulmonary infection, still the nephritis has completely disappeared.

DR. HARTMANN.—You do not really deny the close relationship between nephritis and infection but you are stumped, just as we are, as to what to do about the infection when it becomes chronic. In a given case with chronic progressive active nephritis when diseased nasal sinuses are found, one can treat and attempt to cure them, but it may not be possible to do that.

DR. ALDRICH.—In the vast majority of our chronic nephritics, we could not find an infection during the major part of the disease. We have never seen a true case of chronic nephritis that recovered following removal of infected foci. This should be attempted, however, from the standpoint of their general health.

DR. HARTMANN.—I think it is extremely important to give these patients a diet such as Dr. Aldrich has outlined and we have done so for a while. So do Van Slyke, Addis, Peters and Bulger, but I think it would be a mistake to forget that infection is the cause of the trouble.

DR. ALDRICH.—I would say the infection was not necessarily the cause but it would be eliminated anyway.

DR. HARTMANN.—We can find the infection usually, but cannot do so much in eliminating it.

DR. ALDRICH.—I think there is one other thing we ought to emphasize about the difference between adult and childhood nephritis. The commonest type of nephritis in childhood is the rarest type in adults, acute postinfectious nephritis. Moreover, practitioners among adults are seeing in addition to nephritis, the effects of many degenerative changes in the body.

I am as much an admirer of Addis' and Van Slyke's work as Dr. Hartmann is, but I feel they are dealing with a different organism, from the standpoint of growth and recuperative powers and perhaps with an entirely different type of disease. That is why in the original paper from which this abstract has been written, I have said in the summary that what I am saying applies to this disease in children: that which occurs in adults may not be the same thing.

DR. HARTMANN.—I agree that when you take the chronic nephritis in adults, most of it will be arteriosclerotic nephritis, but these cases of Longcope's were all of the postinfectious glomerular type and they who did not recover were certainly like children.

DR. ALDRICH.—Did not the fact that their recuperative powers were less have something to do with the fact that they did not recover?

DR. HARTMANN.—Or possibly the particular type of streptococcus causing the trouble may have been worse. This year we have had a large epidemic of acute hemorrhagic nephritis. We had more cerebral manifestations and myocarditis than ever before.

DR. McKHANN.—We have had the same thing, plus large numbers of mild ones. I have been inclined to separate nephritis and myocarditis; they seem to run separate. Myocarditis seems to have some influence on the kidneys, still that influence is difficult to evaluate and is not necessarily of great importance.

DR. HARTMANN.—Myocarditis occurs during the acute stage when toxicity is great and some of our patients looked as if they had enormous livers.

DR. McKHANN.—Part of the renal lesions might have been due to passive congestion.

DR. HARTMANN.—But they had high blood pressures.

DR. MOODY.—I would like to ask a question as to classification of these cases. Would those be classed as chronic nephritis who show albumin without other symptoms?

DR. ALDRICH.—We would not classify a child with chronic albuminuria as a nephritic unless we found disturbances of function or other symptoms. In our cases there were none that had merely albuminuria; all had other findings or a history of definite symptoms. In fact, simple albuminuria is a very common thing in childhood.

DR. HARTMANN.—But if he persists in having albuminuria, isn't that a type in which you would want to rule out casts?

DR. ALDRICH.—I certainly would, but many such cases do not show abnormalities other than the albumin.

DR. McKHANN.—We have run tests on sediment counts and I do not believe have normal sediment counts.

DR. HARTMANN.—But have you not found this again and again in ward patients when ordinary urine examination showed practically no albumin and the student or interne said they had no blood or casts, that when you checked with sediment counts, you found lots of them? They are called cured and are really in the latent stage.

DR. McKHANN.—I do not think there is any question about type when you speak about chronic active nephritis. Our experience is they go ahead and succumb eventually; whether or not they follow acute infections I think is debatable. The interesting thing to me is whether Dr. Aldrich is dealing with the same type Dr. Hartmann is describing and we are thinking about. If he is, I think his studies on diet are quite remarkable, because efforts to relieve these patients by removing foci of infection and other therapeutic measures we have tried heretofore have been totally unavailing.

DR. ALDRICH.—My patients all had edema, hypertension, albuminuria, blood and casts in the urine, so I think you would have to classify them as the chronic active type.

DR. HARTMANN.—From the time Peters and Bulger published their studies and Van Slyke's monograph came out, we have fed our chronic active nephritics in pretty much the same way you have outlined, still without a particularly good effect. We have not forced vitamins, but have given a general diet. That has been the routine for a number of years.

DR. ALDRICH.—I think most clinics are now doing that. I have no idea as to the specific factor, it may be any one of a lot of things, but it seems to me that since we are not getting anywhere by the treatment of focal infection, it might be well for us to lay more emphasis on other possible factors. I think it is not a misstatement to say that most physicians throughout the country are still treating chronic nephritics with a low protein regime and public opinion tends to keep them that way.

DR. HARTMANN.—How do you feel now about the relationship between infection and nephrosis?

DR. ALDRICH.—For some reason or other, we have seen very few lately but I have always felt that exacerbations in nephrosis were likely to be associated with mild upper respiratory infections. Have you had that experience?

DR. HARTMANN.—We have seen some, some with marked infection and no history. Knowing the susceptibility of these patients to infections, we do not know whether infection is the cart or the horse.

DR. ALDRICH.—That is the way I feel about the chronic nephritics. The incidence of the disease in dispensaries only is a very important point. I have seen but one in private practice and that in consultation.

DR. WILEY JONES (DENVER).—May I tell you what we are doing in Denver not directly in connection with nephrosis but in the study of children generally? Through the Childhood Council, Inc., under the directorship of Dr. Alfred Washburn, we are attempting to start the study of physical condition at the first hours after birth and to trace children as long afterward as we are able to do so. There are about twelve departments under the leadership of various men, each interested in his special field and intensive work has been going on for about ten years, on some two or three hundred children, in a cross-section of the richest and the poorest in a town of about 300,000. Our oldest child is ten or eleven, that means he has undergone a very intensive study once a month or every two months, from every angle it is possible to approach a child. There are many conditions of the kidneys and chest, especially tuberculous conditions, that I think we can prove were laid down very early in infant life. We have felt that the wrong time to study the etiology of disease is after the person has become an adult and we are attempting to begin at the other end.

At the present time a tremendous lot of work has been done upon the lymphatics and kidneys. We have been working on the head and kidneys and we want to start soon on the chest. The lymphatics themselves are proving a very rich field of investigation and we have found many evidences of disease or infection.

DR. MCKHANN.—I would like to ask Dr. Aldrich about the volume of urine voided on the full diets in those with polyuria. Was there any improvement?

DR. ALDRICH.—Yes, there was clinically, although since most of the patients were ambulatory in the dispensary, we do not have accurate records on this point. Three or four are clinically well as far as we can tell.

The meeting adjourned at 4:30 P.M.

Comments

THE action to disband the Central States Pediatric Society, taken at the recent meeting in September, is a matter of more than passing interest. For a society to pass into a stage of desuetude and break up is not uncommon. The situation with the Central States was quite different. Founded seventeen years ago it has been one of the most active of our pediatric groups and one with a loyal enthusiastic membership. Starting with a small group who planned to meet each year in one of the larger clinic centers in the Middle West to *see* what the other men were doing, the demand for membership from men in the smaller cities became so great that the character of the organization was changed and the Society grew to approximately three hundred members. Geographically it finally embraced the entire Mississippi Valley from Duluth to New Orleans and from the Appalachians in the East to the Rocky Mountains in the West. The original character of the meetings has remained unchanged in that the program has been given by the group in the city in which the meeting took place and has been essentially clinical in character. Formal papers have been frowned upon and frequently as many as fifteen presentations have been made at each of the three half-day sessions. While questions were permitted, discussion was taboo. To any one who has watched the growth and activity of the Society during these seventeen years, its influence upon pediatrics in the Middle West is beyond question. To say nothing of its purely professional value it has led to friendships and acquaintances among men in the same field of work over a large territory which were of the greatest value during these past fifteen years when pediatrics has grown so rapidly as a specialized field of practice.

While many watched the passing of the "Central States" with regret, the action was one that has been under consideration for three years and was unanimously agreed upon. Over 90 per cent of the active membership and approximately 25 per cent of the associate membership were members of the Academy of Pediatrics. The annual fall meeting of the Central States will be replaced by an annual meeting of Region III similar in character to those which have been so successful and worth while in these past seventeen years. It is simply a case of change to meet changing times and conditions. In the same way that the "Central States" welded together the pediatricians of the Middle West, so the Academy of Pediatrics is steadily bringing together the men in our field throughout the country. While many voted to disband with regret, personal and sentimental reasons were outweighed by the feeling of obligation to the field of pediatrics as a whole which the Academy represents.

In its seventeen years of activity the "Central States" was built into an active and worth-while organization which exerted an important influence in the field of pediatrics. The Regional Committee of Region III has a duty and obligation to develop an annual Regional meeting which will in every way be as interesting as that of the organization it replaces.

The Journal of Pediatrics

CONTENTS FOR NOVEMBER, 1933

Original Communications

Vitamin A Deficiency in Infants. Kenneth D. Blackfan, M.D., and S. Burt Wolbach, M.D., Boston, Mass. ---- 679

Prolapse of the Rectum in Children. Warren R. Rainey, M.D., St. Louis, Mo. 707

Denver's Infant Mortality. F. P. Gengenbach, M.D., Denver, Colo. ---- 718

Idiopathic Dilatation of the Common Bile Duct in Children. Robert E. Gross, M.D., Boston, Mass. ---- 730

Vulvovaginal Diphtheria. Mark J. Wallfield, M.D., and Abraham M. Litvak, M.D., Brooklyn, N. Y. ---- 756

Purulent Parotitis in the Newborn. Theodore O. Elterich, M.D., Pittsburgh, Pennsylvania ---- 761

Jacob Heine and His Contribution to Poliomyelitis. John Ruhräh, M.D., Baltimore, Md. ---- 765

Common Sense in Infant Feeding. William M. Happ, M.D., Los Angeles, California ---- 772

Chorea in the Negro Race. Harold C. Lueth, Ph.D., M.D., and Don C. Sutton, M.S., M.D., Evanston, Ill. ---- 775

Antiques of Pediatric Interest. T. G. H. Drake, M.B., F.R.C.P. (C) ---- 779

Critical Review

Neurologic Conditions in Infants and Children. R. Cannon Eley, M.D., Boston, Mass. ---- 781

American Academy of Pediatrics

Proceedings Third Annual Meeting of the American Academy of Pediatrics... 797

Comments

Comments ---- 812

THE *Importance of Vitamins*
IN THE DIETARY

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